IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

ARBUTUS BIOPHARMA CORPORATION and GENEVANT SCIENCES GmbH, Plaintiffs, v. MODERNA, INC. and MODERNATX, INC., Defendants.	)	C.A. No. 22-252-MSG
MODERNA, INC. and MODERNATX, INC., Counterclaim-Plaintiffs, v. ARBUTUS BIOPHARMA CORPORATION and GENEVANT SCIENCES GmbH, Counterclaim-Defendants.	)	[redacted]

JOINT CLAIM CONSTRUCTION BRIEF

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I. PLAINTIFFS' INTRODUCTION

Unlike typical claim construction proceedings, in which parties fiercely dispute the meaning of words amenable to multiple interpretations, the parties here generally agree that the terms at issue use straightforward language with a clear meaning. The disputes arise because Moderna seeks to redraft the claims to include requirements that the claims simply do not recite.

1. The claims recite a "particle" with various lipids. Moderna refuses to accept the plain language of "particle," seeking to limit the claim to the "finished" particle that is not subject to any further processing. This temporal limitation violates both controlling precedent, *Exxon Chem. Patents v. Lubrizol Corp.,* 64 F.3d 1553, 1558 (Fed. Cir. 1995), and the patent's disclosure that the invention includes particles subject to further manufacturing processes.

2. Moderna casts aside the plain meaning of the numerical percentages of lipids in the claims, ignoring the "standard scientific convention" of significant figures and rounding, *Viskase Corp. v. Am. Nat'l Can Co.*, 261 F.3d 1316, 1320 (Fed. Cir. 2001), thereby construing "the endpoints of [a] claimed range with greater precision than the claim language warrants," *U.S. Philips Corp. v. Iwasaki Elec. Co.*, 505 F.3d 1371, 1377 (Fed. Cir. 2007).

3. Even where the claims manifestly omit a numerical limitation, Moderna seeks to impose one by importing language from the specification—the "cardinal sin" of claim construction. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1320 (Fed. Cir. 2005) (en banc).

4. And Moderna seeks to confuse, rather than to clarify, the claims of an asserted patent that recites percentages of "fully encapsulated" material. The claim language, read in context and through the skilled artisan's lens as the law requires, refutes Moderna's professed confusion and effort to use claim construction to conjure an indefiniteness defense.

Plaintiffs' constructions, by contrast, reflect the plain meaning of the claims in light of the intrinsic evidence and should be adopted.

II. MODERNA'S INTRODUCTION

For more than a decade, Moderna had been pioneering a new class of medicines made of messenger RNA ("mRNA") and its proprietary lipid nanoparticle ("LNP") technologies. Moderna invested years of work to develop LNPs that function to protect mRNA and deliver it into cells. Plaintiffs did not invent Moderna's COVID-19 vaccine, the mRNA technology upon which it is based, nor the LNP technology that delivers it. Instead, Plaintiffs' Asserted Patents focus on lipids containing very different types of nucleic acid—plasmid DNA and siRNA—***not*** mRNA. Yet, Plaintiffs attempt to expand the scope of their patents to cover Moderna's pioneering technology.

The asserted family of Molar Ratio Patents claim priority to an application filed in 2008.[1] They claim nothing new: four-component lipid systems were known long before 2008. *See, e.g.*, J.A. 52 (U.S. Patent No. 6,287,591) ("Charged therapeutic agents encapsulated in lipid particles containing four lipid components," issued Sept. 11, 2001). The only allegedly novel feature of the Molar Ratio Patents is the purportedly "***surprising discovery***" that particles with higher molar amounts of cationic lipid above 50 mol % and lower amounts of polyethylene glycol ("PEG")-lipid conjugate below 2 mol % "provide advantages" over the overlapping ratios in the prior art. J.A. 1 ('069 Patent) at 5:44–51.[2] Because the commercial formulations of Moderna's COVID-19 Vaccine contain lipids in amounts that fall outside of the claimed ranges, Plaintiffs ask the Court to construe the claims to cover lipid ratios they did not invent. However, each of Plaintiffs' arguments are contradicted by the intrinsic record.

First, Plaintiffs ask the Court to expand the numerical ranges recited in the claims under

[1] The '069, '359, '668, '435, and '378 patents ("**Molar Ratio Patents**") share a common specification. Moderna does not concede that any Asserted Patent is entitled to the priority dates on the face of the patents.

[2] All emphasis added, except where otherwise stated.

the guise of "standard scientific convention," ignoring that they disclaimed any variability years earlier when they deleted "about" from the claimed ranges. *Second*, to avoid prior art in a related *inter partes* review ("IPR"),[3] Arbutus[4] steadfastly maintained that the claims refer to the lipid amounts in the "***finished*** lipid particle" (*i.e.*, the output of manufacturing), rather than the starting materials. Now, to try to cover Moderna's COVID-19 Vaccine, Plaintiffs ignore their earlier position [redacted] *Third*, with respect to the '378 Patent, which Plaintiffs opportunistically filed in the midst of the pandemic and only after Moderna's product was in use by patients, Plaintiffs seek to escape their explicit disclaimers of particles with less than 50 mol % of cationic lipid. Plaintiffs' contradictory positions across these claims should not be permitted. Black-letter law, including prosecution disclaimer, prohibits such tactics. *See Aylus Networks, Inc. v. Apple Inc.*, 856 F.3d 1353, 1360 (Fed. Cir. 2017).

Plaintiffs also assert U.S. Patent No. 9,504,651 (the "'651 Patent"), which expired earlier this year, and purports to claim priority back to an application filed in 2002. J.A. 5 at Cover. The specification of the '651 Patent family focuses on encapsulation of one type of nucleic acid: plasmid DNA. J.A. 5 ('651 Patent) at 14:9–18:61 (Examples 1–8). mRNA appears just ***once*** in the entire specification, in a laundry list definition of "nucleic acids." *Id.* at 3:50–4:3. It was not until 2014, over a decade after Arbutus's provisional application and after Moderna's founding with a

[3] Moderna disagrees with Plaintiffs' overbroad statement that Moderna is estopped from raising arguments based on the prior art. 35 U.S.C. 315(e); Br. at 6. Moderna intends to rely on prior art formulations that Arbutus disclosed before the priority date that could not have been raised in the IPRs, as well as obviousness-type double patenting defenses over Arbutus's earlier patents which have claimed ratios that are patentably indistinct from the asserted claims.

[4] "Arbutus" refers to Arbutus Biopharma Corp. and its predecessors Protiva Biotherapeutics Ltd and Tekmira Pharmaceuticals Corp. Arbutus is a part owner of Genevant Sciences GmbH.

singular focus on making mRNA medicines a reality,[5] that Arbutus decided to seek broad and unsupported claims to lipid compositions comprising mRNA—seemingly to try to capture Moderna's and others' technology. The only purported novel feature of those composition claims is that they require certain percentages of "fully encapsulated" mRNA. The term "fully encapsulated" should be construed consistent with the sole definition in the specification, in which the inventors contrasted "full" encapsulation with "partial." Plaintiffs ignore the term "fully" and instead improperly seek to turn composition claims into method claims.

In sum, Plaintiffs turn a blind eye to the intrinsic record of the Asserted Patents to propose unsupported constructions. Moderna respectfully requests that the Court adopt its proposed constructions, which are in line with the intrinsic record.

III. PLAINTIFFS' INTRODUCTION IN REPLY

Having now seen the validity of many of the asserted claims confirmed three times—by the Patent Office in allowing the claims, by a unanimous panel from the Patent Trial & Appeal Board in response to Moderna's IPR challenges, and then by another unanimous panel of the Federal Circuit on appeal—Moderna knows that proving invalidity is practically impossible and, for its primary invalidity defenses, statutorily estopped. Moderna likewise sees the proverbial writing on the wall on infringement; it would not have undertaken and maintained its expensive PTAB challenges and appeals without knowing its mRNA vaccines, including for COVID-19, contain particles with molar ratios that infringe the asserted claims.

Under the guise of claim construction, Moderna therefore seeks to redraft the claims, all the while accusing Plaintiffs of expanding them. Br. 2-4. Plaintiffs do not seek to expand their

[5] J.A. 78 (*Moderna Announces $40 Million In Financing To Advance Development Of New Biotherapeutic Modality: mRNA* (Dec. 6, 2012)).

claims; they simply seek legally mandated claim constructions that confirm the claims mean what they say. Quite unusually, the plain meaning of the claim language is undisputed here—Moderna does not and cannot dispute that it accords with Plaintiffs' constructions.

In urging its severely constricted constructions, Moderna violates the most fundamental principles of controlling law: by ignoring specification disclosures refuting its constructions, by reading limitations from the specification into the claims, and by rewriting the admittedly clear plain language in the absence of clear and unmistakable disavowal of the particular subject matter it seeks to exclude. As to the critical issue of what the intrinsic record means, Dr. Thompson's expert declaration testimony explains the specification and file history disclosures through the lens of the POSA—the only meaning that matters. J.A. 7 (Thompson) ¶¶ 39-99. Had Dr. Thompson advanced an interpretation that diverged from the POSA's, Moderna surely would have submitted a responsive expert declaration. Moderna declined to do so. Rather, Moderna invites this Court to reinterpret—often quite implausibly—the specification and file history through the lens of its own attorneys rather than the POSA. The Court should decline the invitation.

IV. DISPUTED TERMS

A. "mol % of the total lipid present in the particle"

Plaintiffs' Proposed Construction	Moderna's Proposed Construction
Plain and ordinary meaning, *i.e.*, "mol % of the total lipid present in the particle" The recited "mol %" ranges are understood to encompass their standard variation based on the number of significant figures recited in the claim.	"__ mol % of the total lipid present in the finished lipid particle" Where the asserted claims do not recite "***about*** __ mol %," Moderna contends that the recited "__ mol%" ranges are understood as the exact ranges recited in the claim.
'069 Patent, Claims 1, 8, 15, 20, 21; '359 Patent, Claims 1, 7, 9, 10, 11, 12, 13, 18, 19; '668 Patent, Claims 1, 8, 10, 15; '435 Patent, Claims 1, 4, 7, 8; '378 Patent, Claims 1, 2, 7, 13, 18, 24, 25	

1. Plaintiffs' Opening Position

The inventions described and claimed in the patents-in-suit tackled the most challenging

problem that had vexed the field for decades: how to deliver nucleic acid (such as DNA or mRNA) therapeutics to cells, where they can exert their desired effect, without being degraded by enzymes in the bloodstream. Five of the asserted patents, U.S. Patent Nos. 8,058,069 (the "'069 patent"), 8,492,359 (the "'359 patent"), 8,822,668 (the "'668 patent"), 9,364,435 (the "'435 patent"), and 11,141,378 (the "'378 patent") (together, the "Lipid Composition Patents"), claim novel nucleic acid-lipid nanoparticles ("LNPs") that are particularly well suited to protect and deliver nucleic acid, such as the mRNA in Moderna's vaccine, to their intended cellular targets. Without the LNPs, the mRNA would degrade rapidly in the body and be ineffective. In addition to the nucleic acid, these particles are comprised of specified lipid components: a "cationic" lipid, which exhibits a positive charge under certain conditions; one or two "non-cationic" lipids, such as a phospholipid or cholesterol; and a "conjugated" lipid, such as a polyethyleneglycol (PEG)-lipid, that inhibits aggregation of particles. *E.g.*, '378 patent, 48:30-59:23; J.A. 7 (Thompson) ¶¶ 18-21. The ***ratio*** of the lipid components—typically expressed on a mole[6] percent (mol %) basis of the total lipid in the particle—affects the physicochemical and biological properties of the LNPs. The patents disclose and claim novel lipid ratios that result in LNPs having excellent efficacy and tolerability.

Moderna previously challenged two of the Lipid Composition Patents (the '069 patent and the '435 patent) in *inter partes* review ("IPR") proceedings. The Patent Trial & Appeal Board rejected Moderna's challenge with respect to all claims of the '069 patent, as well as claims 7, 8, 10, 11, 13, and 16-20 of the '435 patent. Moderna's ensuing appeals to the Federal Circuit failed, leaving it estopped from advancing defenses based on the prior art. 35 U.S.C. § 315(e).

The first term at issue is clear and requires no construction. Moderna does not dispute the clarity of the language, but attempts to rewrite the claims to suit its litigation position in two ways.

[6] A mole ("mol") is a measure of the amount of a substance, based on the number of molecules.

First, although the claim recites only a "particle," Moderna seeks to insert a temporal limitation that the particle must be "finished" and not subject to further processing. This position is contrary to the claim language and specification, and violates longstanding precedent requiring claim terms to be given their "full scope" absent a "clear disavowal." *Thorner v. Sony Comput. Ent. Am. LLC*, 669 F.3d 1362, 1365-66 (Fed. Cir. 2012). *Second*, Moderna seeks to impose an impossible degree of precision to the recited ranges, such that a particle containing even 0.001% less than the claimed lower endpoint—a number that ordinarily would be rounded to be within the claimed range—would fall outside the range. Neither the claims nor the intrinsic record support Moderna's effort to eliminate any degree of rounding, which is contrary to the "standard scientific convention" of significant figures and rounding, *Viskase*, 261 F.3d at 1320, and Federal Circuit precedent that "the endpoints of [a] claimed range" "should not be read . . . with greater precision than the claim language warrants," *Iwasaki*, 505 F.3d at 1377.

a. Moderna's construction impermissibly adds the word "finished."

Each claim of the Lipid Composition Patents requires a "nucleic acid-lipid particle." Moderna proposes to add the word "finished," hoping to narrow the claims to a "finished product" or a "final nucleic acid-lipid particle" that does not undergo any further manufacturing steps. J.A. 30 (Invalidity Contentions), 138-40. That position is contrary to the plain claim language and the specification, which does not limit the claimed particle to any specific stage of the manufacturing process. Rather, to fall within the claim, the particles need only to be formed.

That is clear from the claims themselves. The plain claim language only requires a nucleic acid-lipid particle, without any limitation as to how the particle is formed, when in the manufacturing process it is formed, or whether it is subjected to further processing. This alone disposes of Moderna's argument. *Homeland Housewares, LLC v. Whirlpool Corp.*, 865 F.3d

1372, 1375 (Fed. Cir. 2017) (claim construction "begins and ends" with the claim language).

That result is also confirmed by the specification, which expressly defines "lipid particles" and "stable nucleic acid-lipid particles." *E.g.*, '378 patent, 11:42-12:8, 57:59-64, 59:25-32. During the '435 patent IPR, the PTAB adopted a definition of a "nucleic acid-lipid particle"—"a particle that comprises a nucleic acid and lipids, in which the nucleic acid may be encapsulated in the lipid portion of the particle"—consistent with the definitions disclosed in the specification. J.A. 28 ('435 Patent Final Written Decision, IPR2018-00739, Paper No. 51 at 10-11 (P.T.A.B. Sept. 11, 2019)). The specification's definitions are legally controlling, *Phillips*, 415 F.3d at 1315, and they do not require that the particles not be subject to further processing. To the contrary, the specification expressly discloses embodiments where nucleic acid-lipid particles can be further modified after formation. For example, the specification discloses the addition of salts "after the particles have been formed," '378 patent, 61:46-47; inserting a cationic-polymer-lipid conjugate ("CPL") into a "pre-formed" particle, *id.*, 62:11-13; and "sizing" "the lipid particles of the invention" with sonication, homogenization, or extrusion, *id.*, 61:4-32. The attached declaration of Dr. David Thompson, an expert with decades of experience in the field, explains that the person of ordinary skill in the art ("POSA") would understand the specification to disclose, repeatedly, embodiments of "particles" that are subject to further manufacturing steps and processing. J.A. 7 (Thompson) ¶¶ 40-52. Under Moderna's construction, these embodiments—which the specification calls "particles"—would be excluded, and only the last-in-time particle would be within the scope of the claims. *Id.* However, "it is incorrect to construe the claims to exclude th[ese] embodiment[s]." *Oatey Co. v. IPS Corp.*, 514 F.3d 1271, 1277 (Fed. Cir. 2008).

Where the specification discusses particles subject to further processing, it does not exclude them from the nucleic acid-lipid particles of the invention or distinguish them from particles *not*

subject to further processing steps. The word "finished" never modifies "lipid particles" anywhere in the specification or claims. That word is used only in the context of the "Finished Product Characterization" in Tables 2, 4, 6, and 7, as shown, for instance, below:

TABLE 2

Characteristics of the SNALP formulations used in this study.

Sample No.	Formulation Composition, Mole % PEG(2000)-C-DMA | DLinDMA | DPPC | Cholesterol	Lipid/Drug Ratio	Finished Product Characterization		
			Size (nm)	Polydispersity	% Encapsulation
1	2 | 40 | 10 | 48	12.4	57	0.07	90
2	1.8 | 36.4 | 18.2 | 43.6	14.0	72	0.12	89
3	1.4 | 27.0 | 6.8 | 64.9	16.5	70	0.12	92
4	1.3 | 25.3 | 12.7 | 60.8	18.1	76	0.07	93

This portion of the specification undermines Moderna's position, because it confirms that the patentee knew how to use the term "finished," but did not do so, with respect to the claimed "nucleic acid-lipid particle." *See Core Wireless Licensing S.A.R.L. v. LG Elecs., Inc.*, 880 F.3d 1356, 1366 (Fed. Cir. 2018). Moreover, as Dr. Thompson explains, the POSA would have interpreted the word "Finished" in these Tables as distinguishing the ***formed*** particles from the ***starting materials*** used to make those particles, consistent with other portions of the specification. J.A. 7 (Thompson) ¶ 51; *e.g.*, '378 patent, 61:48-62:58 (distinguishing nucleic acid to lipid ratios "in a formed SNALP" from "the ratio of the starting materials"), 25:55-59, 70:32-43 (noting that certain lipid ratios are "target formulations").

Moderna's proposed construction also contravenes established precedent that, absent disavowing language in the specification, it is erroneous to interpret claims to "read only on [an] end product." *Exxon,* 64 F.3d at 1558; *Astra v. Andrx*, 222 F.Supp.2d 423, 540-41 (S.D.N.Y. 2002). Because "[t]he specification as a whole, and the claims in particular, contain no temporal limitation," the claims only require that a particle "exist[] during manufacture that is being used to make the end product." *Exxon*, 64 F.3d at 1558; *Andrx*, 222 F.Supp.2d at 541 ("Should the HPMCP-salt layer in Andrx's ANDA products form during the enteric coating process or after

manufacture, those products still infringe."). The claims recite a particle with a lipid composition, whenever made. *Exxon*, 64 F.3d at 1558 (claims were "to a composition that contains the specified ingredients ***at any time*** from the moment at which the ingredients are mixed together").

The prosecution history is in accord. It does not support Moderna's proposed temporal limitation, much less provide the requisite "clear and unmistakable disavowal" of claim scope. *Thorner*, 669 F.3d at 1366. Moderna relies on Plaintiffs' statement during the IPR proceedings that "the finished particle must be tested to determine its final composition." J.A. 30 (Invalidity Contentions), 138-39. Moderna ignores the relevant context surrounding these statements, which again makes clear that Plaintiffs were only distinguishing between the ***formed particles*** and the ***starting materials*** used to make those particles—as the specification does. They were not excluding from the claimed invention particles subject to further processing steps.

Specifically, during the IPR proceedings, Moderna argued that the prior art disclosed a formulation with ratios encompassing those claimed in the Lipid Composition Patents. J.A. 7 (Thompson) ¶ 53. In response, Plaintiffs argued that the publication did not disclose the claimed nucleic acid-lipid particle, because it described lipid starting materials, not any particles formed from those starting materials. *Id.* ¶¶ 53-55. Plaintiffs explained that testing of the "finished" particles thus was necessary, because the composition of a formed particle may differ from the composition of the lipid starting materials used to make the particle. *Id*. This discussion provides no support for Moderna's effort to exclude from the claim formed particles that are subjected to further manufacturing or processing steps. *Id*. The claims mean what they say— a "particle," not a "finished" or "final" particle that cannot be subjected to further processing. *Id.* ¶ 55.

b. The recited ranges follow the standard scientific conventions of significant figures and rounding.

Moderna further errs by rewriting the ordinary meaning of the mol % ranges recited in the

claims to be "exact." The Federal Circuit repeatedly has held that the plain meaning of numbers in claims adheres to the "standard scientific convention" of significant figures and rounding. *Viskase*, 261 F.3d at 1320; *Iwasaki*, 505 F.3d at 1377. Significant figures are the digits in a number that indicate its precision, such that when compared to other numbers expressed with additional digits, those other numbers are rounded to the last significant figure. J.A. 7 (Thompson) ¶¶ 22-24; J.A. 38, 103; J.A. 39, 3-4. The number "0.91" thus encompasses values "between 0.905 and 0.914, based on the reasoning that numbers in this range would be rounded to 0.91." *Viskase*, 261 F.3d at 1320; *Iwasaki*, 505 F.3d at 1377 ("'1.0' may be said to have more significant digits than '1' with no decimal point," and thus "[i]t is technically incorrect to assert" a "greater precision" than what is "reflected in the recitation of a significant digit following the decimal point."); *see also Par Pharm., Inc. v. Eagle Pharms., Inc.*, 44 F.4th 1379, 1382 (Fed. Cir. 2022) (affirming judgment regarding claims requiring "a rounded pH between 3.7-3.9, *i.e.*, a pH between 3.65-3.94 before rounding"). District Courts, including in Delaware, regularly apply this rule when applying ranges in patent claims. *E.g.*, *Actelion Pharms. Ltd. v. Mylan Pharms., Inc.*, 2022 WL 446788, at *5 (N.D. W. Va. Feb. 14, 2022) ("a pH of 13 or higher" "encompass[es] those values that round up or down to 13, 12.5 to 13.4"); *Noven Pharms., Inc. v. Actavis Labs. UT, Inc.*, 2016 WL 3625541, at *3 (D. Del. July 5, 2016) ("15 mg mg/cm^2" means "15 plus or minus at least .5"); *Par Pharm., Inc. v. Eagle Pharms. Inc.*, 2021 WL 3886418, at *3 (D. Del. Aug. 31, 2021); *Johnson Matthey Inc. v. Noven Pharms., Inc.*, 2009 WL 2208214, at *7, *9 (E.D. Tex. July 21, 2009) (construing "41-42° C" to have its "literal range" of "between 40.5° C and 42.4° C"). And courts routinely reject efforts like Moderna's to limit numbers and ranges to their "exact" or "precise" limits devoid of any rounding. *See, e.g.*, *Iwasaki*, 505 F.3d at 1377; *Noven*, 2016 WL 3625541, at *3 (construing claim not to require "precisely 15.0 mg/cm^2"); *Unimed Pharms. LLC v. Perrigo Co.*, 2015 WL

1094601, at *6-7 (D. Del. Mar. 11, 2015) ("'exactly' is unnecessary and needlessly adds a limitation" to "1.0% to 10.0% (w/w) of 0.1 N sodium hydroxide"); *Otsuka Pharm. Co. v. Lupin Ltd.*, 2022 WL 2952759, at *2 (D. Del. July 26, 2022) ("I reject any construction intended to connote greater precision than '1 mole per 1 mole' or '0.25 [moles] . . . per 1 mole.'").

This "standard scientific convention" applies to Plaintiffs' claims straightforwardly. Claim 1 of the '069 patent, for instance, recites a "nucleic acid-lipid particle comprising . . . a cationic lipid comprising from 50 mol % to 65 mol % of the total lipid present in the particle." This range and others in the claims would be understood based on the number of significant figures included in the numeric values; here, that means that a value of 49.5 mol % would round up to 50% and be within the range; in contrast, if the claim recited "50.0 mol %," 49.5% *would not* round up, but 49.95% *would* round up (to 50.0%). J.A. 7 (Thompson) ¶¶ 56, 60. Yet Moderna's construction asserts that no rounding applies, so that even 49.999 mol % would ***not*** fall within the claimed range, violating Federal Circuit precedent by "stat[ing] the endpoints of the claimed range with greater precision than the claim language warrants." *Iwasaki*, 505 F.3d at 1377. Nothing in the intrinsic record reflects an intent to deviate from standard scientific convention and limit "50 mol %" to "50.000%"—much less to add an infinite number of trailing zeros as Moderna contends.

To the contrary, the specification reflects an intent to apply the rules of significant figures. Table 2 of the specification specifies ratios using different numbers of significant figures for the lipid components. *E.g.*, '069 patent, 69:16-17. Sample No. 1 is "2"% PEG (conjugated lipid), "40"% DLinDMA (cationic lipid), "10"% DPPC (phospholipid), and "48"% cholesterol. '069 patent, 69:5-50 (Table 2). Sample 10, by contrast, uses "1.**3**"% conjugated lipid, 53.**3**"% cationic lipid, 13.**3**"% phospholipid, and "32.**0**"% cholesterol. *Id.* The trailing zero after the decimal point in "32.0"% cholesterol is especially crucial—it confirms that the inventors used significant figures

as intended: 32.0% conveys a different degree of precision and rounding than 32%. Table 2 reflects this usage repeatedly across every lipid component: Sample No. 3 ("27.**0**"% cationic lipid), Sample No. 7 ("64.**0**" cholesterol), Sample No. 8 ("25.0"% cationic lipid and "60.**0**"% cholesterol), Sample No. 12 ("1.**0**"% conjugated lipid), Sample No. 13 ("7.**0**"% phospholipid). *Id.* And Table 4 reflects the same use of significant figures and trailing zeros in Group No. 8 ("27.**0**"% cationic lipid), and Group No. 10 ("25.**0**"% cationic lipid and "60.**0**"% cholesterol"), while Group Nos. 2, 4, 5, and 13 recite integers with no post-decimal point zeros. *E.g.*, '069 patent, 71:16-17, 71:24-53. There is simply no reason to use numbers like "40" in one instance and "60.0" in another, other than to convey that the latter has more significant digits for rounding purposes than the former. Otherwise, the inventors would have reported the values in the same way, such as 40 and 60. J.A. 7 (Thompson) ¶ 61-63. In that regard, the specification is clear and controlling: it uses additional significant figures, including trailing zeros, to convey additional precision where desired, consistent with rules of rounding. *Phillips*, 415 F.3d at 1316 ("construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be, in the end, the correct construction"). The specification thus does not support adding precision as Moderna proposes. Courts have done so only on the basis that the specification or file history showed that the patentee "relie[d] on [additional] significant figure[s] . . . to distinguish [the invention] from the prior art," *Viskase*, 261 F.3d at 1321-22, "treated [a less precise number] as if it were [more precise]," *id.* ("0.91" g/cm^3 as "0.910" g/cm^3), "repeatedly differentiate[d] between formulations" that would be the same without adding additional significant figures, *AstraZeneca AB v. Mylan Pharms. Inc.*, 19 F.4th 1325, 1329 (Fed. Cir. 2021) (the patent contrasted "0.001% w/w PVP" with "0.0005% w/w PVP"), or where rounding was "impossible" or in irreconcilable "tension" with the specification, *Takeda Pharm. Co. v. Zydus Pharm. USA, Inc.*, 743 F.3d 1359,

1363 (Fed. Cir. 2014). None of those fact patterns applies here. J.A. 7 (Thompson) ¶ 64.

So too, nothing in the file history shows that Plaintiffs used the claimed mol % terms with more precision than the recited number of significant figures, let alone the "clear and unmistakable disavowal of scope" required to displace the ordinary meaning. *Grober v. Mako Products, Inc.*, 686 F.3d 1335, 1341 (Fed. Cir. 2012); *see also Viskase*, 261 F.3d at 1321-22. Moderna relies on a claim amendment that removed the qualifier "comprising about" from certain numerical ranges. J.A. 10 (8/11/2011 Response), 2. Far from disavowing the "standard" rules of significant figures and rounding, as in *Viskase*, 261 F.3d at 1321-22, the amendment was made in direct response to the Examiner's statement that the term "comprising about" could "embrace an amount ***+/- 10, 20, 30 mol %*** of a lipid component." J.A. 9 (5/12/2011 Office Action), 2. The amendment removing "comprising about" did not relate to—let alone disclaim—rounding. *Compare Viskase*, 261 F.3d at 1321-22. And in response to the amendment, consistent with the understanding of the removed "comprising about" language reflected in the rejection, the Examiner withdrew the rejection and allowed the claims. J.A. 10 (8/11/2011 Response); J.A. 11 (9/12/2011 Notice of Allowance). Thus, the removal of "comprising about" as a modifier of "50 mol % to 65 mol %" cationic lipid did not remove rounding, but rather—per the Examiner's explicit statement prompting the amendment—"***+/- 10, 20, 30 mol %*** of a lipid component." This case thereby contrasts starkly with those imposing additional specificity, where the patentee needed to draft claims narrowly to avoid the prior art.[7] J.A. 7 (Thompson) ¶¶ 65-71.

[7] *Jeneric/Pentron, Inc. v. Dillon Co.*, 205 F.3d 1377, 1382 (Fed. Cir. 2000) (patentee "rel[ied] on the ***precise*** ranges of the claims to distinguish" "nearly identical" prior art); *In re Fenofibrate Patent Litig.*, 910 F.Supp.2d 708, 712 (S.D.N.Y. 2012) ("unlikely that this two-hundredths difference would have been enough for the patent examiner to award the patent"). Nor do Plaintiffs seek to read out the claimed ranges, unlike cases like *Talbert Fuel Sys. Patents Co. v. Unocal Corp.*, 275 F.3d 1371, 1374–75 (Fed. Cir. 2002) (patentee sought to negate "345F" from the

Accordingly, the removal of "comprising about" from the claims during prosecution does not support Moderna's construction. It had nothing to do with whether the claimed ranges are entitled to the degree of precision of their literal expression, and thus cannot displace the general rules of significant digit rounding. *See, e.g.*, *Copan Italia S.p.A. v. Puritan Medical Prods. Co.*, 2019 WL 5699078, at *12 (D. Maine Nov. 4, 2019); *Johnson Matthey*, 2009 WL 2208214, at *4, *9 (construing "literal range" of "41-42° C as from "40.5° C" to "42.4° C" despite absence of "about"); *see also* J.A. 7 (Thompson) ¶ 71. There is no basis to adopt Moderna's construction.

2. Moderna's Answering Position

The parties dispute two aspects of this claim term, both of which Plaintiffs improperly attempt to use to expand the numerical scope of the claims. *First*, the claims reciting ranges are properly read to require the precise molar percentages[8] in the claims (*e.g.*, "0.5 mol % to 2 mol %" should not be read to be "0.45 mol % to 2.4 mol %" as Plaintiffs suggest). Plaintiffs gave up any variability when they deleted "about" from the claims during prosecution and when they repeatedly emphasized the narrowness of the ranges to avoid the prior art. *Second*, based on Plaintiffs' explicit and repeated disclaimers, the claims refer to the amount of lipid in the "***finished*** lipid particle," which Arbutus defined as "particles that ***ultimately result*** from the downstream fabrication process." J.A. 72 ('435 Appeal, D.I. 67) at 63–65. Plaintiffs propose "plain and ordinary meaning" to try to avoid their disclaimers.

claim), or to render the claimed ranges "approximations" untethered to the "numerical precision" denoted by the literal text of the claim, unlike cases like *Baxter Healthcare Corp. v. Nevakar Injectables, Inc.*, 2023 WL 4175261, at *15 (D. Del. June 26, 2023).

[8] Molar amount of a substance is the amount of that substance measured in moles. A mole is a unit of measurement to express amounts of a chemical substance. Molar percentage of a lipid in a mixture refers to the proportion of moles of a specific lipid relative to the total moles of all lipids.

a. The claimed ranges should be construed with numerical precision.

Almost all Asserted Claims of the Molar Ratio Patents recite specific amounts of four lipid components using a numerical range of molar percentages ("mol %"), without any "about" qualifier (*e.g.*, "cationic lipid comprising from 50 mol % to 65 mol % of the total lipid present in the particle," J.A. 1 ('069 Patent) at claim 1). In contrast, certain dependent claims recite specific amounts, rather than ranges, and include the word "***about*** __ mol %" (*e.g.*, "about 57.1 mol % cationic lipid" *id*. at claim 14). Examples of both types of claims are shown below:

1. A nucleic acid-lipid particle comprising:
(a) a nucleic acid;
(b) a cationic lipid comprising from 50 mol % to 65 mol % of the total lipid present in the particle;
(c) a non-cationic lipid comprising a mixture of a phospholipid and cholesterol or a derivative thereof, wherein the phospholipid comprises from 4 mol % to 10 mol % of the total lipid present in the particle and the cholesterol or derivative thereof comprises from 30 mol % to 40 mol % of the total lipid present in the particle; and
(d) a conjugated lipid that inhibits aggregation of particles comprising from 0.5 mol % to 2 mol % of the total lipid present in the particle.

14. The nucleic acid-lipid particle of claim **10**, wherein the nucleic acid-lipid particle comprises about 57.1 mol % cationic lipid, about 7.1 mol % phospholipid, about 34.3 mol % cholesterol or a derivative thereof, and about 1.4 mol % PEG-lipid conjugate.

The claims falling in the first category (*i.e.*, those expressed as ranges, which omit the word "about") should be construed with numerical precision to the exact numbers recited in the claim, with no approximation.

1) The claim language and specification confirm the inventors deliberately chose not to claim any degree of approximation.

Based on black-letter law, the claim language mandates that these claims are limited to the precise ranges claimed. Indeed, "the Federal Circuit has made clear that when a patent includes qualifying language for certain claim limitations [such as 'about'] but omits it from others, the claims without such approximation language should be construed with numerical precision." *Baxter Healthcare Corp. v. Nevakar Injectables, Inc.*, C.A. No. 21-1184, 2023 WL 4175261, at *15 (D. Del. June 26, 2023); *id.* ("This construction, assigning numerical precision to composition

ranges, is particularly appropriate when other variables in the same claims explicitly use qualifying language." (quoting *Jeneric/Pentron, Inc. v. Dillon Co., Inc.*, 205 F.3d 1377, 1381 (Fed. Cir. 2000))). Here, the patentee chose to omit words of approximation in the claims that recite ranges but did so in other dependent claims which recite "about" certain percentages. The court in *Baxter* explained that when a patentee does so, a person of skill in the art "would understand that the patentees knew how to express ambiguity in claim language when they so desired." *Id.*

The specification also shows that the inventors knew how to use words of approximation or variability when discussing lipid amounts. *See, e.g.*, J.A. 1 ('069 Patent) at 3:10–20 ("***about*** 50 mol % to ***about*** 85 mol %"), 49:55–62 (same), 24:50–67 (*e.g.*, "about"), 68:39–48 ("Typically, in the 1:57 formulation, the amount of cationic lipid will be 57 mol %±***5 mol %***, and the amount of lipid conjugate will be 1.5 mol %±***0.5 mol %***").[9] The inventors' choice not to omit such words of approximation or variability in the range claims at issue indicates they intended to claim the recited ranges with precision.

2) The prosecution history confirms the patentee's explicit disclaimer of any degree of approximation.

During prosecution of the earliest Molar Ratio Patent, the '069 Patent,[10] the original range claims included words of approximation—*e.g.*, "***about*** 50 mol % to ***about*** 65 mol %." *See, e.g.*, J.A. 55 ('069 P.H. Apr. 15, 2009) at Claims; J.A. 56 ('069 P.H. Nov. 12, 2009) at Claims; J.A. 57 ('069 P.H. June 1, 2010) at Claims; J.A. 8 ('069 P.H. Jan. 31, 2011) at Claims. As shown below in a table submitted by the applicant, prior art reference U.S. Pat. Pub. No. 2006/0008910

[9] Plaintiffs try to avoid drawing attention to the fact that they seek to expand the scope of the claims by a range up to 0.5 mol %. Br. at 12; J.A. 7 at ¶ 60. But, again, when the inventors wanted to allow for variability of 0.5 mol %, they expressly stated that. *See* J.A. 1 ('069 Patent) at 68:39–48 (referring to components as "1.5 mol %±0.5 mol %").

[10] *See* J.A. 80 for a summary table listing the Molar Ratio Patents and related IPR proceedings.

("MacLachlan") taught ranges for the four lipid components that overlapped with the claimed ranges (J.A. 10 ('069 P.H. Aug. 11, 2011) at 8):

Lipid Component	Claim 1 as Amended	US 2006/0008910*
Cationic Lipid	50-65 mol %	"2-60, 5-50, 10-45, 20-40, 30 mol%"
Phospholipid	4-10 mol %	"5-90 mol%"
Cholesterol	30-40 mol %	"20-55 mol %"
Conjugated Lipid	0.5-2 mol %	"1-20 mol %"

The examiner found that the pending claims "read on a broad range of amounts because of the term 'comprising about'" and rejected those claims over the prior art, including MacLachlan. J.A. 9 ('069 P.H. May 12, 2011 Office Action) at 2. To overcome these rejections, the applicant amended claims 1, 9, 21, 47, and 48 (now asserted claims 1, 8 ,15, 20, and 21) to remove the word "about" from the ranges. J.A. 10 ('069 P.H. Aug. 11, 2011) at 2–4:

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1. (Currently amended) A nucleic acid-lipid particle comprising:

(a) a nucleic acid;

(b) a cationic lipid comprising from ~~about~~ 50 mol % to ~~about~~ 65 mol % of the total lipid present in the particle;

(c) a non-cationic lipid comprising a mixture of a phospholipid and cholesterol or a derivative thereof, wherein the phospholipid comprises from ~~about~~ 4 mol % to ~~about~~ 10 mol % of the total lipid present in the particle and the cholesterol or derivative thereof comprises from ~~about~~ 30 mol % to ~~about~~ 40 mol % of the total lipid present in the particle; and

(d) a conjugated lipid that inhibits aggregation of particles comprising from ~~about~~ 0.5 mol % to ~~about~~ 2 mol % of the total lipid present in the particle.

With this amendment, the applicant "point[ed] out that claim 1 as presently amended recites ***narrow*** ranges for each of the lipid components compared to . . . MacLachlan." *Id.* at 8. The applicant also relied heavily on purported "***new and unexpected results***," arguing that the claimed "formulations having increased amounts of cationic lipid, *e.g.*, one or more cationic lipids

comprising from 50 mol % to 65 mol % of the total lipid present in the particle, provide ***unexpectedly superior advantages***." *Id.* at 9 (emphases in original). Following the applicant's removal of "about" and arguments about unexpected results based on the "increased amounts of cationic lipids," the examiner withdrew the rejections and allowed the claims to issue. J.A. 11 ('069 P.H. Sept. 12, 2011 Notice of Allowance). Likewise, for the later Molar Ratio Patents, the applicant narrowed the claims during prosecution by deleting claims reciting ranges with "about" and replacing them with claims mirroring the issued '069 Patent claims.[11] In the related IPR and later Federal Circuit appeal, Plaintiffs repeated the same arguments about the narrowness of the ranges and the importance of the "high levels" of cationic lipid above 50 mol % and "low levels of conjugated lipids" at 0.5–2 mol %. *See* J.A. 72 ('435 Appeal, D.I. 67) at 19 (referring to "the ***surprising discovery*** that nucleic acid-lipid particles with ***high levels of cationic lipids*** and ***low levels of conjugated lipids***") and 64 ("[prior art] L054 has the starting composition including 2% conjugated lipid (PEG-n-DMG), which is ***right at the edge*** of the 0.5 mol % to 2 mol % range claimed in the '435 Patent."); *id.* at 63–65; *see also* J.A. 65 ('069 IPR, Paper 15) at 7; J.A. 67 ('069 IPR, Ex. 2004) at 71; J.A. 68 ('435 IPR, Paper 24) at 14, 35.

Plaintiffs now argue that they only disclaimed broader variability of "+/- 10, 20, 30 mol %" (Br. at 14), but the examiner did not define "about" in this way. Instead, the examiner explicitly noted "about" was ***not*** defined, while observing merely that it "***could*** embrace an amount +/- 10, 20, 30 mol %." J.A. 9 ('069 P.H. May 12, 2011 Rejection) at 2. At no point did the applicant inform the examiner that the claims still allowed some degree of variability. To the contrary, applicant continually emphasized the "narrow" ranges. J.A. 10 ('069 P.H. Aug. 11, 2011 Resp.) at

[11] J.A. 59 ('359 P.H. Oct. 5, 2011 Claims); J.A. 60 ('359 P.H. Mar. 28, 2012 Claims); J.A. 63 ('668 P.H. June 26, 2013 Claims); J.A. 64 ('668 P.H. Nov. 6, 2013 Claims); J.A. 61 ('435 P.H. Aug. 18, 2014 Claims); J.A. 62 ('435 P.H. Feb. 26, 2015 Claims).

7–8. There is no doubt that "had the inventors desired . . . to include a margin of error, they could easily have included the word 'about' in the claim language," as they did for certain dependent claims. *Takeda Pharm. Co. v. Zydus Pharms. USA, Inc.*, 743 F.3d 1359, 1365 (Fed. Cir. 2014).

3) Black-letter law applies to prevent Plaintiffs from rewriting the claims under the guise of "standard scientific convention."

Plaintiffs incorrectly argue that "[t]he recited 'mol %' ranges are understood to encompass their standard variation based on the number of significant figures recited in the claim." D.I. 129 at 10. In *Noven Pharmaceuticals*, the court explicitly rejected this position, where a defendant proposed that the term "coat weight of greater than or equal to 10 mg/cm^2" should be construed as "coat weight of greater than 9.5 mg/cm^2" to include variation based on significant figures. *Noven Pharms., Inc. v. Amneal Pharms., LLC*, C.A. No. 18-699, 2019 WL 1102681, at *4 (D. Del. Mar. 8, 2019). The court disagreed, explaining "there is no [] need to invoke a significant digits analysis because the claims do not recite specific coat weight values but instead a range . . ." *Id*. Here too, the claims recite a mol % range, and thus, no allowance for significant figure analysis is required nor warranted.

Plaintiffs seem to indicate that *U.S. Philips Corp. v. Iwasaki Electric Co.* supports the use of significant figures generally. Br. at 11 But that is incorrect—the Federal Circuit in *Iwasaki* held that the term "between 10^{-6} and 10^{-4} μmol/mm^3" meant expressly that range and explained "[a]lthough the upper and lower bounds of the claimed range are expressed as powers of ten, this alone is ***no reason for treating them as anything other than the ordinary numbers*** that they are." 505 F.3d 1371, 1376 (Fed. Cir. 2007). Likewise, Plaintiffs rely on *Otsuka Pharmaceutical Co. v. Lupin Ltd.* (Br. at 12), but the court in *Otsuka* also expressly rejected "reading a margin of error into the disputed claim term." C.A. No. 21-900-RGA, 2022 WL 2952759, at *2 (D. Del. July 26, 2022). In fact, consistent with Moderna's construction, the court there held that "Defendant is

correct that because the claim term lacks 'broadening words,' the numerical range in this claim involves a 'strict numerical boundary.'" *Id*.

Moderna takes the same position here—*i.e.*, because the claims lack broadening words, the ranges are a strict numerical boundary. *See Jeneric/Pentron, Inc. v. Dillon Co., Inc*., 205 F.3d 1377, 1381 (Fed. Cir. 2000) ("Without broadening words that ordinarily receive some leeway, the precise weight ranges of claim 1 do not 'avoid [] a strict numerical boundary to the specified parameter'") (internal citations omitted); *Baxter Healthcare*, 2023 WL 4175261, at *15 (D. Del. June 26, 2023); *see also TwinStrand Biosciences, Inc. v. Guardant Health, Inc*., C.A. No. 21-1126-GBW-SRF, 2022 WL 17986012, at *11 (D. Del. Dec. 29, 2022), *report and recommendation adopted*, 2023 WL 3773700 (D. Del. June 2, 2023) (construing "comprises between 1 nanogram (ng) and 100 ng of cfDNA molecules" by its plain and ordinary meaning and rejecting attempts to construe it in a manner exceeding the bounds of the "precise numerical range").

Plaintiffs attempt to paint Moderna's construction—which simply holds Plaintiffs to what they claimed—as extreme, because it would not allow for "a particle containing even 0.001% less than the claimed lower endpoint." Br. at 7. But the Federal Circuit has affirmed that such a level of precision is required where, as here, the patentee chose to claim ranges and amounts without words of approximation. *Takeda Pharm.*, 743 F.3d at 1365 ("inventors have consistently relied on 400 μm as ***the dividing line*** between granules that . . . were within the scope of the invention, and those that were not"); *Jeneric/Pentron*, 205 F.3d at 1381 (concluding that where "the ***claim recites precise ranges***" "the district court correctly limited the weight ranges to those ***recited precisely***" in the claim); *AstraZeneca AB v. Mylan Pharmaceuticals Inc.*, 19 F.4th 1325, 1329, 1333–35 (Fed. Cir. 2021) (rejecting construction permitting 0.0005% deviation in light of the intrinsic record and where the inventors removed the qualifier "about" from the claims.).

Plaintiffs cite a litany of cases, but each is inapposite for the reasons discussed below:

- *Viskase* construed claim terms with words of approximation such as "about 0.91 g/cm.^{3}" *Viskase Corp. v. Am. Nat'l Can Co.*, 261 F.3d 1316, 1320 (Fed. Cir. 2001). There is no equivalent term here; indeed, Arbutus removed "about" from the claims during prosecution.

- *Par Pharmaceutical, Inc. v. Eagle Pharmaceuticals Inc.*, 44 F.4th 1379 (Fed. Cir. 2022) and 2021 WL 3886418, at *3 (D. Del. Aug. 31, 2021) involved pH readings where ***both parties agreed*** that a person of skill in the art would round pH readings to the nearest tenth decimal. There is no such agreement here and Dr. Thompson does not suggest mol % is subject to any rounding guidelines in the art. J.A. 7 (Thompson Decl.) ¶¶ 22–24, 56–71.

- *Actelion Pharmaceuticals. Ltd. v. Mylan Pharmaceuticals, Inc.*, 2022 WL 446788, at *5 (N.D. W. Va. Feb. 14, 2022) is also limited to pH readings, where the patentee demonstrated "in the specification that it could measure the pH . . . with increased precision, up to four significant figures." *Id.* at *6. The specification here includes ***no measurements*** of mol % whatsoever, let alone measurements up to any significant figures.

- In *Noven Pharmaceuticals, Inc. v. Actavis Laboratories UT, Inc.*, the substantive dispute was about ***how many*** significant figures should be used, not about whether variability was appropriate at all. 2016 WL 3625541, at *3, *3 n.2 (D. Del. July 5, 2016). Moreover, this case did not involve claimed ranges, let alone ranges where the patentee chose to remove the word "about." *See Amneal Pharms.,* 2019 WL 1102681, at *4 (comparing claims to those in *Actavis* decision, agreeing there was no need "to invoke a significant digits analysis" for range claims).

- In *Johnson Matthey Inc. v. Noven Pharmaceuticals, Inc.*, the parties again ***agreed*** certain rounding principles were appropriate. 2009 WL 2208214, at *4–5 (E.D. Tex. July 21, 2009). The court ultimately permitted a range due to the apparatus used for measurement and without such a range the claims would be indefinite. *Id.* at *8–9. None of these facts apply here.

- *Unimed Pharmaceuticals LLC v. Perrigo Co.* supports Moderna's position. Indeed, the court agreed with defendants' construction, but noted that "'exactly' is unnecessary" because "[t]he Court is not certain what 'exactly' adds that is not captured in the rest of the construction." 2015 WL 1094601, at *7 (D. Del. Mar. 11, 2015). In other words, there was no need to add the "exactly" to the claims because the court read the claims as inherently expressing exact ranges.

- *Copan Italia S.p.A. v. Puritan Med. Prods. Co. LLC* held that "from 90% to 100%" has the plain and ordinary meaning of "between 90% and 100%." 2019 WL 5699078, at *12 (D. Me. Nov. 4, 2019). While Plaintiffs apparently rely on this case because the court did not adopt defendants' construction requiring a precise range, the court did not do so because Plaintiffs never argued the term did not require such precision. In other words, the precision was already baked into the claim language and no further construction was required.

4) Plaintiffs' application of "significant figures" based on extrinsic evidence should also be rejected because it conflicts with the intrinsic record and Plaintiffs' prior positions.

Faced with an overwhelming intrinsic record confirming the claimed ranges are to be construed precisely, Plaintiffs resort to extrinsic expert opinion from Dr. Thompson. Br. at 12. But his purported "standard scientific convention" of significant figures cannot overcome the intrinsic record and well-established claim construction principles discussed above. *See supra* § IV.A.2.a.3. Moreover, Plaintiffs' construction based on purported "standard scientific convention" must be rejected because it conflicts with the intrinsic record and Plaintiffs' prior positions.

First, Plaintiffs bury the full extent of their attempt to broaden the claims in the declaration of Dr. Thompson (J.A. 7 ¶ 60), which confirms they do seek to recapture what they disclaimed:

'069 Patent, Claim 1	Recited Range	Lower Limit	Upper Limit
Cationic Lipid	"50 mol % to 65 mol %"	49.5 mol %	65.4 mol %
Phospholipid	"4 mol % to 10 mol %"	3.5 mol %	10.4 mol %
Cholesterol	"30 mol % to 40 mol %"	29.5 mol %	40.4 mol %
Conjugated Lipid	"0.5 mol % to 2 mol %"	0.45 mol %	2.4 mol %

Stunningly, for the range of "conjugated lipid," Plaintiffs seek to expand the claimed upper limit from 2 mol % to reach 2.4 mol %—a ***20% expansion*** of the 2 mol % limit. This dramatic expansion of 20% is irreconcilable with Dr. Thompson and Plaintiffs' (erroneous) argument that Arbutus only disclaimed "+/- 10, 20, 30 mol %" variation during prosecution when removing the word "about" from the claims. J.A. 7 ¶¶ 68–70, Br. at 14. Instead, this confirms that Plaintiffs ***do*** seek to recapture what they expressly disclaimed when they deleted the word "about," including variation of up to 20%.

Second, Dr. Thompson's selective reliance on certain portions of the intrinsic record does not hold water. For example, he relies on Tables 2 and 4 of the '069 Patent to opine that the applicant knew how to express precision to tenths. Br. at 12–13; J.A. 7 ¶¶ 61–63. But these tables also include rows where the mol % values are ***not*** rounded, which only shows that the patentee knew how to express mol % values with and without decimals and specifically choose to claim the latter. *Id.* ¶¶ 57–59 (replicating '069 Patent Tables 2 and 4).

Third, Dr. Thompson's unsupported approach is contradicted by Arbutus's own arguments interpreting almost identical claim limitations in a European patent from the Molar Ratio Patent family. There, Arbutus argued that prior art teaching 29.5 mol % of cholesterol "falls ***outside*** of the claimed range of 30 mol % to 40 mol %." J.A. 76 (Arbutus Sept. 3, 2018 Brief, EP2279254) at 2 (pending claim 1), 17.[12] Yet here, according to Dr. Thompson's table above (J.A. 7 ¶ 60), 29.5 mol % of cholesterol is ***within*** the scope of ***the same claim limitation***. Plaintiffs' irreconcilable positions confirm they are not applying any "standard" scientific convention. In an effort to expand the claims here, Plaintiffs and Dr. Thompson urge that significant figure analysis should be applied to each ***individual number*** in the claim, which allows for variation of between 0.05 mol % to 0.5 mol %. J.A. 7 ¶ 60. But for the European equivalent, when Plaintiffs wanted to rely on the claim being narrow to avoid to prior art, Plaintiffs argued that "the level of precision of the values" for ***all*** lipid amounts in the claim is determined by the ***most precise number*** in the claim (*i.e.* "0.5 mol %" conjugated lipid) and "that the mol % of the individual components must also be considered to the ***same*** degree of precision." J.A. 76 at 17. If Dr. Thompson applied that to claim 1 of the '069 Patent, the maximum variation for ***all*** lipid components would be 0.05 mol%, because 0.5 mol % conjugated lipid is the most precise number recited in the claim and to which he allowed only 0.05 mol % variability. J.A. 7 ¶ 60. Instead, Plaintiffs depart from this prior approach by applying significant figures to individual numbers in the claim because it allows them to selectively expand the scope of almost all claimed amounts by 0.5 mol % instead of 0.05 mol%.

In sum, Plaintiffs' arguments based on "standard scientific convention" should be rejected because they are at odds with the intrinsic evidence and Plaintiffs' prior positions. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1318 (Fed. Cir. 2005) (en banc) ("[A] court should discount any expert

[12] EP2279254 (J.A. 54) and the Molar Ratio Patents claim priority to U.S. Prov. App. 61/045,228.

testimony that is clearly at odds with the claim construction mandated by the claims themselves, the written description, and the prosecution history. . .") (internal citations omitted).

Regardless, this Court need not decide which of Plaintiffs' varying approaches of rounding is appropriate, because the Federal Circuit and other courts have held that ***no*** significant figure analysis is appropriate for claimed ranges that lack any words of approximation. *See supra* § IV.A.2.a.3. Therefore, the Court should construe the recited ranges as the precise ranges in the claim.

b. The claims recite the lipid amounts in a "finished lipid particle."

The claims of the Molar Ratio Patents recite "a nucleic acid-lipid particle comprising" lipids in varying molar percentages "of the total lipid present in the particle." The claims should be construed to refer to the "mol % of the total lipid present in the ***finished lipid particle***." As Arbutus unequivocally and repeatedly stated during the related IPR, the intrinsic record is clear that the claimed "mol %" refers to the molar percentage in the "finished lipid particles" which it defined as the "particles that ***ultimately result*** from the downstream fabrication process."[redacted] The Court should reject Plaintiffs' "plain and ordinary meaning" proposal, which is yet another a backdoor attempt to improperly recapture leeway in the amount of lipids claimed.

1) Arbutus's clear disclaimer during the IPRs confirms that the claimed "lipid particle" is a "finished particle" *i.e.* the particle that "ultimately results" from manufacturing.

During the '435 Patent IPR and related appeal, Arbutus argued that the claims recite the lipid amounts of a "finished lipid particle," which it defined as the "output formulation," *i.e.* the

particle that "***ultimately result[s]*** from the downstream fabrication process." J.A. 68 ('435 IPR, Paper 24) at 39; J.A. 72 ('435 Appeal, D.I. 67) at 63–65; J.A. 73 ('435 Appeal, D.I. 83) at 1.

Specifically, in an attempt to distinguish the claims from the prior art during the '435 IPR, Arbutus distinguished between "input formulation (*i.e.*, nucleic acid and lipid mixture)" described in the prior art, and the claimed "***output*** formulation (*i.e.*, lipid particle)." J.A. 68 ('435 IPR, Paper 24) at 40. In doing so, Arbutus argued that the specification supported such a reading.[13] *Id*. at 40 ("Even the '435 Patent explains that the lipid-to-drug ratio (i.e., lipid to nucleic acid ratio) calculated from the input components is **not identical to that of the finished product**. *See*, *e.g.*, EX1001 ['435 Patent], 79:50–80:9 (reporting different input and **final lipid to drug ratios for SNALP formulations**) . . ."); *see also* J.A. 69 ('435 IPR, Paper 49) at 26 ("[t]he claims . . . do not recite a starting mixture for making particles"). Arbutus further argued that that the prior art did not anticipate because "[i]t was widely documented in the art that a ***finished particle*** must be tested to determine its composition." J.A. 68 ('435 IPR, Paper 24) at 40; J.A. 28 ('435 IPR, Paper 51) at 22–25. During the '435 IPR, Arbutus argued that its construction of "finished particle" was supported by the "descriptions of particle production methods and extensive characterization of ***finished particles***" in "Tables 2, 4, 6, 7" of the '435 Patent. J.A. 79 ('435 IPR, Paper 34) at 8. Now, Plaintiffs point to the same tables to try to avoid that same construction. Br. at 9.

On appeal, Arbutus again distinguished between input formulations of the prior art and the claims which are directed to finished particles—"the lipid concentrations of the particles that ***ultimately result*** from the downstream fabrication process." J.A. 73 ('435 Appeal, D.I. 83) at 1;

[13] The specification also contrasts amount of lipid "present in the SNALP formulations" as claimed (*i.e.,* lipid content in the finished particle), with the "target" formulation (*i.e.,* input amounts). J.A. 1 ('069 Patent) at 24:64–67; *id.* at 68:35–39. During the IPRs, Moderna's and Arbutus's experts agreed "there is no meaningful distinction" between the claimed "lipid particles" and SNALPs. J.A. 67 ('069 IPR, Ex. 2004) ¶ 45; J.A. 70 ('435 IPR, Ex. 1007) ¶ 61.

J.A. 72 ('435 Appeal, D.I. 67) at 61 (emphasizing "the critical distinction between 1) starting ingredients for making lipid particles; and 2) the different lipid composition of ***particles resulting from the fabrication process***" as claimed), 63–65. Moderna's proposed construction is entirely consistent with Plaintiffs' repeated and explicit disclaimers.[14]

Dr. Thompson now opines that the claimed "particle" "refer[s] to any formed particle, irrespective of whether it was the particle ***in the final drug product*** or whether it would be subjected to additional manufacturing and processing steps." J.A. 7 ¶ 43. However, during the IPR, Dr. Thompson repeatedly opined that the claims recited the amount of the lipid in the "finished product." J.A. 67 ('069 IPR, Ex. 2004) ¶ 112; *id*. ¶ 110 (opining that "input formulation" of the prior art was "something different" from "the ***output*** formulation (*i.e.* lipid particles)," and that "testing of the ***finished*** particle composition is necessary to account for variations in the molar fractions of the lipid components in the ***starting*** lipid formulation.").

The PTAB and the Federal Circuit relied on Arbutus's repeated characterizations of the "finished lipid particle" in assessing patentability. *See* J.A. 28 ('435 IPR, Paper 51) at 22–25; J.A. 75 ('435 Appeal, D.I. 135 (Fed. Cir. Dec. 1, 2021)) at 18. Thus, Arbutus has made a "clear and unmistakable disavowal of claim scope" and should not now be permitted to reclaim that scope. Br. at 10 (citing *Thorner v. Sony Comput. Ent. Am. LLC*, 669 F.3d 1362, 1366 (Fed. Cir. 2012)); *see also Speyside Med., LLC v. Medtronic Corevalve, LLC*, C.A. No. 20-361-GBW-CJB, 2023 WL 4043955, at *5 n.11 (D. Del. June 16, 2023), *report and recommendation adopted*, 2023 WL

[14] Plaintiffs' argument that ***Moderna*** hopes to "narrow the claims" (Br. at 7) is simply incorrect. Construing the claims as being directed to a "finished product" is exactly what ***Arbutus*** advocated for in the IPR. Indeed, in arguing that the claims were limited to "finished particles," Arbutus relied on FDA Guidance recommending (1) labeling "amount of each lipid component used in the formulation based on the ***final form of the product***."; (2) providing "[a]n expression of the molar ratio of each individual lipid . . . in the ***finished formulation***." J.A. 68 ('435 IPR, Paper 24) at 41 (quoting J.A. 71 (Ex. 2013)) (emphasis in original)).

5368888 (D. Del. Aug. 22, 2023) (finding disclaimer where "repeated statements to the PTAB were specific and clear").

[redacted]

[redacted] The Federal Circuit has held that prosecution disclaimer is designed to prevent such tactics—"[e]xtending the prosecution disclaimer doctrine to IPR proceedings will ensure that claims are not argued one way in order to maintain their patentability and in a different way against accused infringers." *Aylus Networks, Inc. v. Apple Inc.*, 856 F.3d 1353, 1360–61 (Fed. Cir. 2017). Arbutus itself argued that prosecution history disclaimer should apply based on its own statements in the IPR, citing *Aylus*. *See* J.A. 66 ('069 IPR, Paper 30) at 5.

Plaintiffs argue that Moderna's construction would exclude purported embodiments in the specification where a "cationic-polymer-lipid conjugate ('CPL')" is added to a preformed "particle." Br. at 8. However, Plaintiffs' disclaimer during the IPR applies even if Plaintiffs disavowed embodiments in doing so. "[W]here the prosecution history requires a claim construction that excludes some but not all of the preferred embodiments, such a construction is permissible and meets the standard of 'highly persuasive evidentiary support.'" *Rheox, Inc. v. Entact, Inc.*, 276 F.3d 1319, 13227 (Fed. Cir. 2002) (finding disclaimer applied, despite excluding certain embodiments); *see also Revolution Eyewear, Inc. v. Aspex Eyewear, Inc.*, 175 F. App'x 350, 356 (Fed. Cir. 2006) ("Although under this interpretation some of the preferred embodiments will be read out of the '913 Patent, this court has recognized that when there is a clear disclaimer during the prosecution history, it may be appropriate to read out the preferred embodiments"). The passages of the specification referring to the addition of salts or sizing of particles (Br. at 8–9) are also irrelevant, since these features are not claimed and Plaintiffs do not allege either would have an effect on lipid amounts. *Id.*

Finally, Moderna's proposed construction is not an improper importation of a temporal limitation (Br. at 1, 7, 9–10), but rather a claim construction—"particles that ultimately result from the downstream fabrication process"—that Arbutus itself embraced to explain the claims to the Patent Office and the Federal Circuit. *See supra* § IV.A.2.b.1. *Exxon* and *Astra* are distinguishable because neither involved disclaimer, whereas here, Arbutus specifically disclaimed any particle "during manufactur[ing]" from the scope of the claimed "lipid particles," leading the PTAB to construe the claims to require "***final*** formulation percentages." J.A. 74 ('435 Appeal, Argument) at 25:23-26:6 (counsel for Arbutus arguing the prior art did not anticipate the claimed particles because the input amounts "can change ***during manufacture***"), 20:23-21:17 (counsel for Arbutus

contrasting input amounts of lipids described in the prior art compared to "outputs" as claimed, "the claims [of the '435 Patent] were ***construed***, and everyone agrees that they addressed the ***final formulation percentages*** . . . [W]e agree with that too. This claim is directed to a . . . final particle"); *Exxon Chem. Patents v. Lubrizol Corp.*, 64 F.3d 1553 (Fed. Cir. 1995); *Astra Aktiebolag v. Andrx Pharms., Inc.*, 222 F. Supp. 2d 423 (S.D.N.Y. 2002).

The Court should prevent Plaintiffs from expanding the scope of the claims to reach what they disclaimed and construe the claims as reciting the specified "mol % of the total lipid present in the finished lipid particle."

3. Plaintiffs' Reply Position

a. Moderna fails to establish that Plaintiffs clearly and unmistakably disavowed particles subject to further processing.

Moderna attempts to rewrite the claims of the Lipid Composition Patents to require "finished" particles not subject to any further processing. Remarkably, while seeking this construction, Moderna disputes very little of Plaintiffs' position. It does not dispute that its construction departs from the plain meaning of the claim language. Br. 7-8. Nor does it dispute that the claim language is clear and lacks the word "finished" or any other language limiting the claimed particles to a specific stage of processing. *Id*. And it does not dispute that its construction would exclude embodiments set forth in the specification, or that the specification expressly defines the claimed "lipid particle[s]" without the additional restriction Moderna proposes.[15] *Id.* This intrinsic record unambiguously demonstrates that Plaintiffs' construction is correct and that the claims should be afforded their plain and ordinary meaning. *Homeland*, 865 F.3d at 1375.

[15] Without supportive expert testimony, Moderna disputes Dr. Thompson's opinion that sizing techniques disclosed in the specification "would have an effect on lipid amounts," Br. 30. This pure attorney argument on a factual issue is entitled to no weight.

Moderna's sole justification for its construction is a disclaimer theory premised on a misreading of statements during an IPR of the '435 patent. None of those statements is inconsistent with Plaintiffs' construction, and none comes close to the Federal Circuit's exacting standard to establish a "clear and unmistakable disavowal" of claim scope. *Thorner*, 669 F.3d at 1366.

Moderna first cites briefing submitted by Plaintiffs to the PTAB and the Federal Circuit referencing "finished lipid particles" and "final particles" to distinguish prior art at issue in the IPR. Br. 25-26. As explained previously, Moderna ignores the context surrounding Plaintiffs' use of these terms. *See id*. 10. During those proceedings, Plaintiffs sought to make a single, clear distinction between formed particles (an "output formulation"), on the one hand, and the disclosures in the prior art relating to the "starting solution" used to make those particles (the "input formulation"), on the other. J.A. 68 ('435 IPR, Paper 24) 39-40; J.A. 7 (Thompson) ¶ 20. In other words, the vials on the shelf with ingredients versus the particles that are later formed using those ingredients. Many of the quotes that Moderna cites evince this very distinction. Br. 25-27; *e.g.*, J.A. 72 ('435 Appeal, D.I. 67), 61 (emphasizing "the critical distinction between (1) starting ingredients for making lipid particles; and (2) the different lipid composition of ***particles resulting from the fabrication process***"). Plaintiffs were only clarifying that the delineation was between starting materials and "***any*** resulting particle," not just particles ultimately included in a pharmaceutical product or those not subject to any subsequent processing, as Moderna now argues. J.A. 68 ('435 IPR, Paper 24), 40. The distinction Moderna now raises—between formed particles subject to further processing and so-called finished particles not subject to further processing, Br. 25-27—was simply not at issue in the IPR, much less the subject of a disavowal. To the contrary, the surrounding context confirms that Plaintiffs' discussion of molar percentages of "finished particles" pertains to "the lipid percentages of the ***formed*** particles," irrespective of when those

"formed particles" arise in the manufacturing pathway. J.A. 73 ('435 Appeal, D.I. 83), 11.

The Board and Federal Circuit readily understood this was the distinction Plaintiffs were making. The Board's Final Written Decision uses the term "finished" in just a single sentence, in the context of differentiating formed particles from "***starting materials***." J.A. 28 ('435 IPR, Paper 51), 22. And the Federal Circuit understood Plaintiffs' arguments to relate to a "critical distinction between ***starting ingredients*** versus a final product," rather than a distinction from particles that underwent further processing. J.A. 75 ('435 Appeal, D.I. 135), 16.

Moderna also relies on Plaintiffs' oral arguments before the PTAB and Federal Circuit. Br. 25-27. But there too Plaintiffs only addressed the differences between starting materials and formed particles. J.A. 69 ('435 IPR, PTAB O.A.), 26 ("The claims are directed to nucleic acid lipid particles . . . they do not recite a starting mixture for making particles."). Before the Federal Circuit, Plaintiffs explained that the prior art only disclosed ratios of starting materials, which did not anticipate the claimed particles because those ratios could change "during manufacture." J.A. 74 ('435 Appeal, CAFC O.A.), 26:1-6. From this, Moderna contends that Plaintiffs "specifically disclaimed any particle 'during manufactur[ing]' from the scope of the claimed 'lipid particles.'" Br. 30. Plaintiffs did no such thing. Moderna omits the remainder of counsel's discussion, which clarifies that the only distinction being made was between the ratios in (1) the starting lipid solution and (2) the formed particle. J.A. 74 ('435 Appeal, CAFC O.A.), 21:13-17 (explaining that the claims cover a "final particle" and "not the inputs of what you put in ***before you manufacture the particle***"). This is consistent with the specification, which makes the very same distinction. Br. 8-9; '069 Patent, 24:64-67, 68:35-39. Moderna identifies no statement suggesting that the claims reach only particles that are not further modified after formation or that the claims are limited to a particular manufacturing stage once a particle exists. That simply was not the issue in the IPR.

Moderna's evidence thus falls far short of the exacting standard for disavowal. "[D]isclaimer or disavowal of claim scope must be clear and unmistakable, requiring 'words or expressions of manifest exclusion or restriction' in the intrinsic record." *Unwired Planet, LLC v. Apple Inc.*, 829 F.3d 1353, 1358 (Fed Cir. 2016). When a patentee's statement "is subject to more than one reasonable interpretation, it cannot rise to the level of a clear and unmistakable disclaimer." *Aylus Networks, Inc. v. Apple Inc.*, 856 F.3d 1353, 1363 (Fed. Cir. 2017). Here, Plaintiffs did not clearly disclaim any formed particles from the scope of the claims, and "the remainder of the specification and the prosecution history shows that [the patentee] did not clearly disclaim or disavow such claim scope." *Rambus, Inc. v. Infineon Techs. AG*, 318 F.3d 1081, 1094-95 (Fed. Cir. 2003). Moderna itself acknowledges that the specification discloses "particles" subject to further processing. Br. 30.

Finally, and remarkably, Moderna cites its ***own*** internal manufacturing document to urge disavowal. Br. 28-29; J.A. 77. This non-public document, "not available to one of ordinary skill in the art, even today," cannot be considered in claim construction. *E.g.*, *Teva Pharm. USA, Inc. v. Sandoz Inc.*, 810 F.Supp.2d 578, 597 (S.D.N.Y. 2011). Nor is there any reason why the POSA would associate ***Moderna's*** document with the interpretation of any claim in ***Plaintiffs'*** patents.

[redacted] Moderna's position now—that a particle formed before the end of a manufacturing process is not a "particle" as that term is used in the patents—is inconsistent with its own usage of the word and the intrinsic record, which

is replete with embodiments of particles subject to further modification. Br. 8.

b. Moderna's construction impermissibly imports an impossible degree of "numerical precision" into the claimed mol % ranges.

Federal Circuit precedent, the intrinsic record, and uncontroverted expert evidence uniformly support Plaintiffs' construction of the claimed mol % ranges to have their plain meaning in accordance with the rules of significant figures and rounding. Moderna's construction defies controlling authority, as the Federal Circuit again clarified just days after Moderna's brief. And Moderna cannot show that Plaintiffs, by removing "about" from the claim, clearly and unmistakably disclaimed all variation, including rounding. The record demonstrates the opposite.

1) Moderna's argument contravenes Federal Circuit precedent.

Decades-old precedent affirms the general rule that rounding is a "standard scientific convention" that applies to claimed ranges, *Viskase*, 261 F.3d at 1320; *AstraZeneca*, 19 F.4th at 1329, and that the "endpoints of [a] claimed range" "should not be read . . . with greater precision than the claim language warrants," *Iwasaki*, 505 F.3d at 1376. Against these controlling precedents, Moderna inveighs that its no-rounding construction is mandated by "black-letter law," Br. 16, 20-22, yet it relies on unpublished trial court decisions in *Baxter* and *Noven.* These cases cannot override *Viskase*, *Iwasaki*, and *AstraZeneca*, and Moderna makes no attempt to show—as the challengers in *Viskase* and *AstraZeneca* did—that the intrinsic evidence prohibits ***any*** variability in the claimed range, no matter how small. *See* Br. 13-14.

Indeed, the ink was barely dry on Moderna's brief when the Federal Circuit squarely repudiated the very propositions for which Moderna cites *Baxter* and *Noven*. Specifically, in *Actelion Pharms Ltd. v. Mylan Pharms. Inc.*, --- F.4th ---, 2023 WL 7289417 (Fed. Cir. Nov. 6, 2023), the court addressed the precise argument Moderna advances here—that "[u]nlike other

claim terms, the disputed claim term lacks approximation language like 'about'" and thus the recited ranges must be read "***exactly***." *Id.* at *4; *compare* Br. 21 ("because the claims lack broadening words, the ranges are a strict numerical boundary"). The Federal Circuit declined what Moderna urges here, to "find the absence of approximation language dispositive" and "reject[ed] any invitation to create a bright-line rule . . . that the lack of approximation language, ***even when it may be found elsewhere in the claims***, dictates a precise value." *Id.*; *see also, e.g.*, *Copan*, 2019 WL 5699078, at *12; *Johnson Matthey*, 2009 WL 2208214, at *4. Likewise, relying on *Noven*, Moderna argues that significant figures and rounding do not apply because the claims recite "ranges" and not "specific . . . values." Br. 20. The Federal Circuit squarely rejected this argument in *Actelion* as well, reaffirming that "there is no blanket rule that ranges . . . must foreclose rounding," and "[t]his is especially true in this case where"—as here—"there is in fact an upper limit in the claim." 2023 WL 7289417 at *3; *see also, e.g.*, *Par*, 44 F.4th at 1382.

The Federal Circuit cases that Moderna cites in passing, *Jeneric/Pentron* and *Takeda*, are not to the contrary. Significant figures and rounding simply were not at issue in those cases—the words "significant figures" and "rounding" appear nowhere in the decisions, and the Federal Circuit never passed on these issues, because neither party proposed a construction relying on or disputing the applicability of rounding. *Jeneric/Pentron*, 205 F.3d at 1382; *Takeda*, 743 F.3d at 1365. Contrary to Moderna's assertion, Plaintiffs' construction defines the claimed mol % ranges with "numerical precision," *Baxter*, 2023 WL 4175261, at *15—the numerical precision that is "warrant[ed]" by the significant figures of the literal "claim language," *Iwasaki*, 505 F.3d at 1377.

Moderna's construction defies "black-letter law," and its assertion that the "Federal Circuit [has] held that no significant figure analysis is appropriate for claimed ranges," Br. 25, is

demonstrably wrong. Controlling precedent mandates adoption of Plaintiffs' construction.[16]

2) The intrinsic evidence establishes the applicability of significant figures and rounding, and Moderna fails to show disclaimer.

Moderna has little response to the specification's use of significant figures, including trailing zeros, to express numeric values with different degrees of precision. Br. 12-13; J.A. 7 (Thompson) ¶¶ 61-63. From the POSA's perspective, the specification unambiguously shows that the rules of rounding apply, not that (as Moderna suggests implausibly) the inventors could express "values with and without decimals." Br. 23. Moderna points to "about" in the specification, but this is not "dispositive," *Actelion*, 2023 WL 4789417, at *4; *Copan*, 2019 WL 5699078, at *12; *Johnson Matthey*, 2009 WL 2208214, at *4. Moderna also relies on the specification's use of "±" ("57 mol %±5 mol %," "1.5 mol %±0.5 mol %"), Br. 17, but this language was used to specify greater variance than significant figures and rounding, making it irrelevant to the parties' dispute.[17]

Moderna thus, again, takes on the heavy burden of showing disclaimer. Here, it urges that Plaintiffs' amendment removing "about" from the claimed ranges constitutes "an explicit disclaimer." Br. 17-18. The file history unambiguously establishes that the Examiner equated

[16] *Actellion* also negates Moderna's attempts (Br. 22) to distinguish cases applying significant figures and rounding. The presence or absence of "about" in *Viskase*, and *Noven v. Actavis*, is not "dispositive." *Actellion*, 2023 WL 7289417, at *3-4. Nor does it matter whether a specific value or a range was at issue. *Id*. *Iwasaki*, *AstraZeneca*, and *Actellion* all addressed ranges where a term of approximation was not recited, and *Viskase* had nothing to do with the meaning of "about." Moderna suggests that the lack of dispute regarding rounding distinguishes *Par*, *Johnson Matthey*, and *Copan*, but claim construction is a legal question for the Court, not the parties, *see Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 384 (1996), and the undisputed application of rounding in these cases underscores the common, uncontroversial application of significant figures and rounding as "standard scientific convention[s]." *Viskase*, 261 F.3d at 1320; *AstraZeneca*, 19 F.4th at 1329. Finally, Moderna criticizes the lack of evidence relevant to rounding in *Par* and the district court decision in *Actelion*, but ignores extrinsic evidence (Dr. Thompson's declaration), which the Federal Circuit deemed "highly relevant" in *Actelion*. *Infra* § IV.A.3.b.3).

[17] "1.5 mol %±0.5 mol %" is not inconsistent with Plaintiffs' construction as Moderna contends. Br. 17 n.9. "1.5" has a rounding range of 1.45 to 1.54, narrower than "1.5 mol %±0.5 mol %."

"about" with "+/- 10, 20, 30 mol %," that Plaintiffs amended the claims to obviate this reading, and that the Examiner thereafter allowed the claims. Br. 14-15. None of the language Moderna cites from the file history concerns rounding. Br. 17-19. And Plaintiffs' statements characterizing the claimed ranges as "narrow" were merely a comparison to claims the Examiner understood to permit a variation of "+/- 10, 20, 30 mol %." Neither those statements, nor anything else during prosecution, had anything to do with significant figures or rounding. *See* Br. 48-51; *infra* § IV.B.3.

Moderna responds that the Examiner "did not define 'about' in this way," Br. 19, but that is belied by Moderna's position and expert testimony in the IPR. In asserting that claim 14 of the '069 patent (which recites "about") was invalid, Moderna and its experts adopted the "+/- 10, 20, 30 mol %" meaning of "about" set forth by the Examiner, rather than significant-digit rounding:

> Claim 14, recites specific lipid concentrations, but includes the term "about"—which implicates a range. While [Patent Owner] argues that "this claim is drawn to a 1:57 particle" during prosecution, ***the examiner stated in this context that "'comprising about' could embrace an amount ±10, 20, 30mol% of a lipid component. This would result in ranges far wider*** than those addressed above for the independent claims.

J.A. 82 ('069 IPR Reply), 22-23; J.A. 83 ('069 IPR Petition), 63 ("the 'about' language in this limitation encompasses amounts ±10, 20, 30 mol%"); J.A. 84 (Janoff) ¶¶ 134, 173 (same); J.A. 85 (Anchordoquy) ¶ 111 ("'comprising about' could embrace an amount ±10, 20, 30 mol% of a lipid component"). Moderna fully understood the Examiner's application of "comprising about" as "+/- 10, 20, 30 mol %" and so too would the POSA. Br. 14-15; J.A. 7 (Thompson) ¶¶ 65-71.

Moderna offers no evidence contradicting Dr. Thompson's opinion that the POSA would interpret the claims in accordance with "standard scientific convention[s]," consistent with Plaintiffs' construction. J.A. 7 (Thompson) ¶¶ 56, 60, 65-71; *infra* § IV.A.3.b.3. The discussion of "about" during prosecution had nothing to do with rounding or significant figures and cannot

give rise to a "clear" and "unmistakable" surrender of, for example, 49.999 mol % from the scope of the claims. *Viskase*, 261 F.3d at 1320; *Thorner*, 669 F.3d at 1367.

3) Moderna's attorney argument against rounding is unsupported by expert testimony on an issue where such evidence is "highly relevant."

Actellion did not merely rebuff Moderna's proposed legal framework, it also underscored Moderna's clear evidentiary deficiency. It has long been the law that "[c]laim terms must be construed as they would be understood by a person of ordinary skill" and "[w]hat the claim terms would mean to laymen is irrelevant." *Searfoss v. Pioneer Consol. Corp.*, 374 F.3d 1142, 1149 (Fed. Cir. 2004); *Endoheart AG v. Edwards Lifesciences Corp.*, 2016 WL 1270127, *8 (D. Del. Mar. 31, 2016) (rejecting that counsel's characterization of the claims is "probative" of a POSA's understanding); *Phillips*, 415 F.3d at 1313 ("the [POSA] [reads the intrinsic record] with an understanding of [its] meaning in the field"). In *Actellion*, the Federal Circuit emphasized that this is particularly true as regards the application of significant figures and rounding, where extrinsic evidence (such as expert testimony concerning how the scientific literature and authoritative texts should be applied to claimed ranges) was deemed "highly relevant." 2023 WL 7289417, at *3.

That holding dooms Moderna's position. Dr. Thompson's unrebutted testimony as to the meaning of the intrinsic evidence to the POSA and how "lipid concentrations [are] experimentally determined" totally refutes Moderna's attorney argument. J.A. 7 (Thompson) ¶¶ 22-24, 56-71; J.A. 38, 103; J.A. 39, 3-4; J.A. 42, 1872; J.A. 43, 282, 284; Br. 12-14. Moderna's decision not to respond stands out all the more because Moderna, not Plaintiffs, seeks to deviate from the claims' plain meaning. *Chamberlain Grp. v. Lear Corp.*, 516 F.3d 1331, 1338 n.2 (Fed. Cir. 2008).[18]

[18] Moderna wrongly claims that "Dr. Thompson does not suggest mol % is subject to any rounding guidelines in the art." Br. 22. He opined that the "POSA would have known that mol % values . . . are subject to numerical uncertainty, and would have interpreted the claimed mol % ranges . . . using the standard convention of significant figures and rounding." J.A. 7 (Thompson) ¶ 56.

In lieu of expert evidence supporting its position, Moderna offers only baseless criticisms of Dr. Thompson's and Plaintiffs' supposedly inconsistent "prior positions." Br. 22-25. Moderna accuses Plaintiffs of "bury[ing] the full extent of their attempt to broaden the claims" with respect to the mol % of the conjugated lipid, but at the same time reproduces a table from Dr. Thompson showing clearly Plaintiffs' construction. Br. 23 (quoting J.A. 7 (Thompson) ¶ 60). Moderna's complaint of a "20% expansion" in the conjugated lipid range ("from 2 mol % to reach 2.4 mol %"[19]) merely observes that even small variations can be comparatively large on a percentage basis when applied to small numbers—a mathematical truism. Crucially, Moderna conflates its "20***%*** expansion" of the conjugated lipid range, Br. 23, with the Examiner's statement equating "comprising about" with "+/- 10, 20 30 ***mol %***," J.A. 9 (5/12/2011 Office Action), 2. The two statements refer to percentages of different things. The Examiner's application of "comprising about" was expressly stated in terms of "***mol %***," not a percentage of the claimed range—meaning that "comprising about" 2 mol % from the file history had an upper limit of at least 2 mol % + 10 mol % = ***12 mol %***. 12 is not 2.4, and is not close to the rounding permitted by Plaintiffs' proposal.

Moderna next accuses Dr. Thompson of "selective reliance" on the intrinsic record. Br. 23. But Dr. Thompson fully considered the claims, specification, and the file history together. *See, e.g.*, J.A. 7 (Thompson) ¶¶ 57-70 (citing '069 patent, 18:40-46, 22:30-42, 69:24-45, 71:24-53, 91:26-27; J.A. 8 (1/31/2011 Reply); J.A. 9 (5/12/2011 Office Action); J.A. 10 (8/11/2011 Response); J.A. 11 (9/12/2011 Notice of Allowance)); *Searfoss*, 374 F.3d at 1149; *Phillips*, 415 F.3d at 1313. If the POSA would have interpreted the intrinsic record differently, Moderna could have offered an opposing expert to say so. It did not.

[19] The value "2.4" follows because the POSA would "consider only one digit in the decimal place to the right" for rounding. J.A. 7 (Thompson) ¶ 10. For "2 mol %," that is the tenths decimal place, and any digit in that position equal to or less than 4 would round down (to 2 mol %).

Moderna's criticism also misses the point. That the "patentee knew how to express mol % values with and without decimals and specifically chose to claim the latter," Br. 23, is irrelevant. The question here is the specification's meaning to the POSA, including the "numerical precision" of the claims based on significant figures and rounding, *Baxter*, 2023 WL 4175261, at *15. The patentee expressed mol % with a certain number of significant figures, adding more when desiring greater precision (as in certain values in the specification) and not adding them when not desiring more precision. Br. 12-13; '069 patent, 69:5-50 (Table 2), 71:24-53 (Table 4); J.A. 7 (Thompson) ¶¶ 61-63. Courts must credit the specification, not ignore it as Moderna urges. *Phillips*, 415 F.3d at 1316 ("The construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be, in the end, the correct construction.").

Finally, Moderna criticizes Dr. Thompson's opinions as inconsistent with arguments Arbutus made in European opposition proceedings filed in 2018 by Moderna and Merck. Br. 24. Incredibly, Moderna fails to advise the Court that, in those proceedings, Moderna "expressly agree[d] with, support[ed], and fully adopt[ed]," J.A. 86, 5, that the "regular rules for the rounding of numbers" were applicable to the foreign claims at issue, and that "the value of 29.5 mol-% is thus to be rounded up to 30 mol-%" with respect to a range of "30 mol-% to 40 mol-% of cholesterol or a derivative thereof," J.A. 87, 14-15.[20] Notwithstanding its emphatic affirmation of Plaintiffs' construction in Europe, Moderna now hypothetically speculates based on Arbutus's arguments in that foreign forum—relying solely on attorney argument, without expert testimony—that the "maximum variation" in the mol % ranges would be just "0.05mol%." Br. 24. Whatever its basis, that assertion is entitled to no weight, as Moderna did not offer a "different expert[]" to

[20] In the European proceedings, Merck and Moderna were referred as "Opponent 1" and "Opponent 2" respectively, and variations of these monikers ("O1," "O2," "OA1," "OA2").

"resolve[] th[is] issue[] of fact." *Teva Pharms. USA, Inc. v. Sandoz, Inc.*, 574 U.S. 318, 330 (2015). Regardless, "the theories and laws of patentability vary from country to country, as do examination practices," and controlling "precedent cautions against indiscriminate reliance on the prosecution of corresponding foreign applications in the clai construction analysis." *AIA Eng'g Ltd. v. Magotteaux Int'l S/A*, 657 F.3d 1264, 1279 (Fed. Cir. 2011) (quoting *Heidelberger Druckmaschinen AG v. Hantscho Com. Prods., Inc.*, 21 F.3d 1068, 1072 n.2 (Fed. Cir. 1994)); *Lindemann Maschinenfabrik GMBH v. Am. Hoist & Derrick Co.*, 730 F.2d 1452, 1458 n.2 (Fed. Cir. 1984) ("[T]he language and laws of other countries differ substantially from those in the United States."). The Federal Circuit's extensive precedents on rounding and significant figures for the endpoints of claimed ranges in *Viskase*, *Iwasaki*, *AstraZeneca*, and *Actelion* provide an unambiguous framework to resolve the parties' dispute—not European law. Under this framework, both the intrinsic and extrinsic evidence compel adoption of Plaintiffs' construction.

4. Moderna's Sur-reply Position

a. The claimed mol % ranges do not include variability.

Plaintiffs incorrectly argue that Moderna urges a bright-line rule regarding words of approximation. Not so. Rather, the claims are not entitled to any approximation based on the intrinsic record and Federal Circuit precedent that *Actelion* left intact. Dr. Thompson's extrinsic opinions are entitled to no weight because they are inconsistent with the intrinsic record, Arbutus's past positions, and his earlier testimony, each of which undermine Plaintiffs' arguments that their construction is based on supposedly universal rounding principles.

Claims. Moderna does not dispute that the Federal Circuit in *Actelion* declined to create a bright-line rule for rounding—"either that language like 'precisely' or 'exactly' is always needed to avoid rounding or that the lack of approximation language, even when it may be found elsewhere in the claims, dictates a precise value." 85 F.4th at 1171. But *Actelion* does not warrant rejection

of Moderna's construction. Moderna's argument begins with analysis of the claims; a necessary first step in claim construction. Then, as in *Actelion*, Moderna explained that the specification and file history also demand a construction that does not expand the scope of the claims that were previously narrowed. Nothing in Moderna's approach is contrary to Federal Circuit precedent. *See Takeda*, 743 F.3d at 1362, 1365 (reversing construction that imported "deviation" or "standard of error" into claims). Plaintiffs suggest that because *Actelion* rejected a bright-line rule regarding the absence of words of approximation, rounding based on significant figures ***must*** apply. Br. at 35–36. But that is exactly what *Actelion* rejected—a bright-line rule.

Confusingly, Plaintiffs continue to rely on *Viskase*, *Iwasaki*, and *AstraZeneca*, but these cases are inapplicable. *See* Br. at 20–22. The claims in *Viskase* included words of degree ("about"). Br. at 22. Although Plaintiffs claim that *Actelion* confirms this is not dispositive of implying a range (Br. at 37 n.16), this is inaccurate. *Actelion* explained that where there are no words of degree, there is no bright-line rule. *Actelion*, 85 F.4th at 1171–72. *Actelion* did not state that a Court should ignore words of degree where they exist, as Plaintiffs urge here. To do so would lead to the illogical rewriting of claims. And neither *AstraZeneca* nor *Iwasaki* support the use of significant figures. *AstraZeneca*, 19 F.4th at 1329, 1332–35; *Iwasaki*, 505 F.3d at 1376. Plaintiffs point out that "significant figures" / "rounding" appear nowhere in *Jeneric* and *Takeda* (Br. at 36), but that only confirms Plaintiffs' construction should be rejected. If those principles were "standard scientific convention" for interpreting ranges, they undoubtedly would have been discussed.

Specification. The specification also demonstrates that the inventors knew how to express approximation and precision. While Plaintiffs argue the inventors "expressed mol % with a certain number of significant figures, adding more when desiring greater precision (as in certain values in

the specification) and not adding them when not desiring more precision," this only supports Moderna's argument—when the inventors desired less precision, they indicated that with "about" or "±_ mol%," which are noticeably lacking in the claims. Br. at 41.

Prosecution History. In *Actelion*, "the prosecution history d[id] not provide clarity." 85 F.4th at 1173. Here, it does. During prosecution, Arbutus removed "about" from the range claims, and in doing so disclaimed approximation. Br. at 15. Plaintiffs' vague characterizations made in hindsight contradict the clear and unambiguous statements made during prosecution. There, the Examiner found the claims "read on a broad range of amounts because of the term 'comprising about.'" J.A. 9 at 2. To overcome this art, Arbutus removed "about" from the claims and "point[ed] out that claim 1 as [] amended recites ***narrow*** ranges for each of the lipid components compared to . . . MacLachlan," and relied on purported "new and unexpected results." J.A. 10 at 4, 9. Plaintiffs now ignore these statements. Moreover, there is no evidence that the Examiner understood the amendments to "equate[] 'about' with '+/- 10, 20, 30 mol %,'" aside from unsupported attorney argument. Br. at 38; Br. at 19–20; J.A. 9 at 2. And, as explained below, even Plaintiffs' expert admitted that he has no opinion on how "about" modified the claims.

Extrinsic Evidence. Plaintiffs argue that *Actelion* deemed "extrinsic evidence (such as expert testimony . . .)" "highly relevant," "particularly . . . regard[ing] the application of significant figures and rounding." Br. at 39. But *Actelion* explained that "***[o]nly if*** a disputed claim term remains ambiguous after analysis of the intrinsic evidence should the court rely on extrinsic evidence." 85 F.4th at 1174. Unlike *Actelion*, here the intrinsic record is clear that the inventors knew how to express words of degree and chose to disclaim any variability.

Even if extrinsic evidence is required, Dr. Thompson's inconsistent opinions are unreliable. Br. at 24. Plaintiffs state that "Dr. Thompson fully considered the claims, specification, and the

file history together" (Br. at 40), but he admitted that he had "not given thought to" the "impact of removing the word 'about' during prosecution." J.A. 88 (Thompson Tr.) at 65:20–66:2. Even worse, he was unable to confirm whether the scope of claim 1 of the '069 patent was narrowed ***at all*** by the removal of "about" or explain what "about" meant in claim 14. *Id*. at 62:15–63:11 (meaning of "about" would depend on many variables), 64:10–23, 65:10–66:2, 67:9–12 ("about" allows for an "indeterminate amount" of variability), 69:9–14 (admitting he did not know how a POSITA would define "about"), 72:18–78:18. This dooms any reliance on his testimony, as he failed to consider the impact of this pivotal change.

Dr. Thompson now interprets the breadth of these claims based on significant figures but previously testified that the breadth of the same claim depended on the precision of an analytical method. *Compare* J.A. 89 (2020 Thompson Dep.) at 146:6–14 (explaining scope of the mol% limitation in '069 claim 1 was "tied to the precision of the measurement [tool]") *with* J.A. 88 at 37:19–20 (stating "significant figures" are "agnostic about the technique that's being used to make that measurement"). Moderna need not offer evidence contradicting Dr. Thompson's opinion; Dr. Thompson contradicts himself. Br. at 38. Such extrinsic evidence, which is inconsistent with the intrinsic record, is entitled to no weight. *Phillips*, 415 F.3d at 1318.

Plaintiffs do not deny taking two irreconcilable positions on supposedly "standard" rounding principles: contending that 29.5 mol% falls both within and outside the ***same*** claimed range (30 to 40 mol %). J.A. 76 at 17; J.A. 7 ¶ 60. Unable to explain this inconsistency, Plaintiffs argue Arbutus's earlier statements about its European counterpart should be disregarded because "theories and laws of patentability vary from country to country." Br. at 42. If Plaintiffs are correct that rounding is determined as a matter of law, then Dr. Thompson's opinions are not

needed.[21] If, on the contrary, his opinions are needed, they are unreliable because there are ***no*** "standard" rounding principles given Plaintiffs' irreconcilable positions. Br. at 24; J.A. 88 at 42:24–43:18 (confirming rounding does not differ overseas).

Given the clear intrinsic record, the recited ranges should be construed precisely.

b. Arbutus defined "particle" as a "finished lipid particle."

Plaintiffs' revisionist history of the IPRs does not change their disclaimer. Plaintiffs admit that references to "finished" and "final" particles were used to distinguish prior art in the IPR. Br. at 32–33. Those statements inform the construction of "particle" here. Rather than dispute that the claims are directed to a "finished particle," Plaintiffs attempt to reinterpret what "finished" means. *Id.* Moderna, the PTAB, the Federal Circuit, and this Court can only take Arbutus at its word based on its prior definitional statements: "***particles resulting from the fabrication process***" (J.A. 72 at 61); those that "***ultimately result from the downstream fabrication process***." J.A. 73 at 1. Moderna does not (and need not) rewrite the claims—Arbutus already defined them.

Plaintiffs suggest that the line drawn in the IPRs was between the starting materials and "any resulting particle." Br. at 32. Yet in the same paragraph from which Plaintiffs quote, Arbutus defines "any resulting particle" as an "***output*** formulation," "***finished*** product," and "***final*** lipid to drug ratios." J.A. 68 at 40. This is not a distinction that "Moderna now raises" but one Arbutus made years ago. Br. at 32. Plaintiffs' statement that the "Final Written Decision uses the term 'finished' in just a single sentence" is misleading. *Id.* at 33. Aside from that sentence explaining Dr. Thompson distinguished prior art based on "less cholesterol [] incorporated in ***the finished particles***," the decision refers to the particle as "***final***" five times (J.A. 28 at 22, 23, 25 (n.10)), the

[21] This Court can properly consider Arbutus's admission that the same claim in Europe is to be construed uniformly based on the most precise number (*i.e.*, the same variability of +/-0.05 mol% applying to ***all*** numbers in the claim). *Gillette Co. v. Energizer Holdings, Inc.*, 405 F.3d 1367, 1374 (Fed. Cir. 2005) (holding party to "blatant admission" in argument made to EPO).

Federal Circuit refers to the particle as "***final***" or "***completed***" eight times (J.A. 75 at 16, 17, 18), and Arbutus and Dr. Thompson made disclaiming statements on at least six occasions. *E.g.*, J.A. 68 at 39–41; J.A. 69 at 26; J.A. 79 at 8; J.A. 67 at ¶¶ 110, 112; J.A. 72 at 61, 63–65; J.A. 73 at 1.

Moderna does not argue that "particles" may not undergo some further processing (*e.g.*, sizing),[22] but that the "final formulation" is the output, not an intermediate step part-way through manufacturing.[23] This is not just Moderna's position—Arbutus first made this distinction in the IPRs. J.A. 74 at 25:23-26:6 (Arbutus's counsel arguing prior art did not anticipate claims because input amounts "can change ***during manufacture***"); *see also id.* at 20:23-21:17. Plaintiffs agree. Br. at 33.[24] Plaintiffs attempt to distract from their prior disclaimer of what a "particle" is by focusing on what it is not, but this bakes in a logical fallacy. That the "particle" is not the starting lipid solution has little bearing on what the particle is; only Arbutus's affirmative, definitional statements explain the line that Plaintiffs agree they previously drew—"particles that ultimately result from the downstream fabrication process." J.A. 72 at 61. Arbutus's repeated disclaimers were "clear and unmistakable" and should apply here. *Aylus*, 856 F.3d at 1360–61.[25]

[22] Plaintiffs' expert was unsure if the molar amounts in Table 4 of the specification are pre- or post-sizing; thus, these embodiments are not excluded under Moderna's construction. J.A. 88 at 101:1–9; 105:2–20. Additionally, Dr. Thompson testified that the Molar Ratio Patents do not teach that those processes change the molar amounts of lipids. *Id.* at 99:6–9.

[23] Moderna's manufacturing process (Br. at 34) was used to explain why the "plain and ordinary meaning" of "particle" is insufficient to resolve the parties' dispute. *O2 Micro*, 521 F.3d at 1361.

[24] Plaintiffs are incorrect that the distinction between "formed" and "finished particles" was "not at issue in the IPR." Br. at 32. Still, Arbutus's disclaimers apply even if "unnecessary to overcome" a reference. *Unicorn Energy GMBH v. Tesla Inc.*, 2023 WL 322891, *4–*5 (N.D. Cal. 2023) (IPR statements binding even if PTAB did not rely on them) ("PTAB's decision leaves intact [] representations regarding the scope of its claims"; "[c]ompetitors are entitled to rely on [them]").

[25] *Unwired* (Br. at 34) is inapplicable. Unlike Arbutus's repeated disavowal before the PTAB, *Unwired* rejected disclaimer based on a single sentence in the specification. 829 F.3d at 1358.

B. "a cationic lipid having a protonatable tertiary amine"

Plaintiffs' Proposed Construction	Moderna's Proposed Construction
Plain and ordinary meaning, *i.e.*, "a cationic lipid having a protonatable tertiary amine"	"a cationic lipid having a protonatable tertiary amine comprising 50 mol % or more of the total lipid present in the finished lipid particle"
'378 Patent, Claim 1	

1. Plaintiffs' Opening Position

The sole dispute concerning this term involves Moderna's attempt to add a requirement to claim 1 of the '378 patent that is not there: that the "cationic lipid" must comprise "50 mol % or more of the total lipid present in the finished lipid particle." Moderna commits the "cardinal sin" of claim construction, by importing language from the specification. *Phillips*, 415 F.3d at 1320. The intrinsic evidence unambiguously demonstrates that claim 1 includes no such limitation.[26]

"It is a 'bedrock principle' of patent law that 'the claims of a patent define the invention.'" *Id.* at 1312. Claim 1 of the '378 patent does not include a limitation related to the mol % of the cationic lipid. By contrast, claim 1 and numerous dependent claims ***do*** recite explicit mol % limitations related to ***other*** lipid elements. *See* '378 patent, claims 2, 7, 13, 18, 24, 25, 29. The patentee knew how to include lipid mol % limitations and chose not to do so for the cationic lipid component of the claim. *See Hill-Rom Services, Inc. v. Stryker Corp.*, 755 F. 3d 1367, 1372 (Fed. Cir. 2014) (claims must "not be read restrictively unless the patentee has demonstrated a clear intention to limit the claim scope using words or expressions of manifest exclusion or restriction").

The claims in the Lipid Composition Patents underscore the point. The cationic lipid limitations in claim 1 of those patents are reproduced below.

Patent	Cationic Lipid Limitation of Claim 1
'069 patent	(b) a cationic lipid comprising from 50 mol % to 65 mol % of the total lipid present in the particle

[26] Moderna's proposed construction also improperly imports a "finished" limitation into the claims. That effort is improper for the reasons discussed above in Section IV.A.1.a.

Patent	Cationic Lipid Limitation of Claim 1
'359 patent	(b) a cationic lipid comprising from 50 mol % to 65 mol % of the total lipid present in the particle
'668 patent	(b) a cationic lipid comprising from 50 mol % to 65 mol % of the total lipid present in the particle
'435 patent	(b) a cationic lipid comprising from 50 mol % to 85 mol % of the total lipid present in the particle
'378 patent	(b) a cationic lipid having a protonatable tertiary amine

Every other patent includes an express cationic lipid mol % limitation. "It is settled law that when a patent claim does not contain a certain limitation and another claim does, that limitation cannot be read into the former claim." *HW Tech., LC v. Overstock.com, Inc.*, 758 F.3d 1329, 1333 (Fed. Cir. 2014). That other patents' claims recite cationic lipid mol %—but not claim 1 of the '378 patent—is dispositive. *E.g.*, *Arlington Indus., Inc. v. Bridgeport Fittings*, 632 F.3d 1246, 1254-55 (Fed. Cir. 2011) (refusing to import "split" limitation recited in a claim of parent patent); *Eis, Inc. v. Intihealth Ger GMBH*, 2023 WL 346631, at *3 (D. Del. Jan. 9, 2023) ("connection element" should not be read into all claims, where it was recited in some patents but not others).

Other claim language of the '378 patent further refutes Moderna's effort to read in a nonexistent mol % limitation. Claim 1 recites "a mixture of a phospholipid and cholesterol of from 30 mol % to 55 mol % of the total lipid present in the particle." Moderna's construction, requiring at least 50 mol % cationic lipid, would truncate the upper limit (55 mol %) of this combined phospholipid/cholesterol range, which is explicitly allowed by the claims. *Phillips*, 415 F.3d at 1314 ("the claims themselves provide substantial guidance as to the meaning of particular claim terms"). Such a rewriting is impermissible. *Helmsderfer v. Bobrick Washroom Equip., Inc.*, 527 F.3d 1379, 1383 (Fed. Cir. 2008) ("Courts do not rewrite claims[.]").

The specification likewise confirms Plaintiffs' proposed construction. The specification provides an express definition for the term "cationic lipid," which is bereft of any requirement as to the amount of cationic lipid in the claimed particles. '378 patent, 13:20-39. That explicit

definition "controls." *Martek Biosciences Corp. v. Nutrinova, Inc.*, 579 F.3d 1363, 1380 (Fed. Cir. 2009). Although the patent discloses particles with over 50 mol % cationic lipid, it refers to those particles as "one aspect" or "some embodiments" of the invention, '378 patent, 3:36-45, 19:22-57; they are not definitions of the invention or the term "cationic lipid." *Martek*, 579 F.3d at 1381 ("[P]articular embodiments appearing in the written description will not be used to limit claim language that has broader effect."). Those exemplary disclosures fall far short of the "clear and unmistakable disclaimer" required to disturb the ordinary meaning of "cationic lipid," *Thorner*, 669 F.3d at 1366-67, let alone displace the specification's definition, which is controlling as a matter of law, *Martek*, 579 F.3d at 1380. Moreover, the specification discloses embodiments with a noncationic lipid (*e.g.*, phospholipid and cholesterol) of greater than 50 mol %, which means that the cationic lipid necessarily would be under 50 mol %. *E.g.*, '378 patent, 20:19-34, 52:59-63 ("In embodiments where the lipid particles contain a mixture of phospholipid and cholesterol . . . , the mixture may comprise up to about . . . 55, or 60 mol % of the total lipid present in the particle."). These disclosures confirm that the patentee did not intend to require 50 mol % or more cationic lipid, as Moderna's proposed rewrite would do.

The prosecution history also supports Plaintiffs' position. The language of claim 1 was present in the original application, J.A. 12 (4/12/2021 Claims), 121, and remained the same throughout prosecution. In rejecting the claims initially, the Examiner did not suggest that the claims included an unwritten cationic lipid mol % limitation; rather, she only discussed the amounts of PEG, phospholipid, and cholesterol. J.A. 13 (6/14/2021 Non-Final Rejection), 7. In response, the applicant likewise did not argue that the Examiner failed to cite prior art related to the amount of cationic lipid; rather, the applicant only addressed the amounts of PEG, phospholipid, and cholesterol. J.A. 14 (8/20/2021 Response), 8-9. The applicant explicitly

distinguished between the cationic lipid component—which the claim requires, but not in any specific amount—and the PEG, phospholipid, and cholesterol components—for which the claim recites particular concentrations. *See id.* at 10 ("none of the references teaches or suggests . . . RNA delivery using a lipid particle containing a cationic lipid ***with phospholipid, cholesterol, and PEG-lipid components at the recited concentration ranges***."). The prosecution history therefore reflects that both the Examiner and applicant understood claim 1 not to require a particular mol % of cationic lipid. *Arlington Indus.*, 632 F.3d at 1255; *Phillips*, 415 F.3d at 1317 ("the prosecution history can often inform the meaning of the claim language by demonstrating how the inventor understood the invention"); *Cooper Notification, Inc. v. Twitter, Inc.*, 867 F.Supp.2d 485, 492 (D. Del. 2012).

By contrast, during the prosecution of the '069 patent—which ***does*** recite a particular amount of cationic lipid—the applicant ***did*** distinguish the prior art based on the concentration of cationic lipid, among other elements. *E.g.*, J.A. 10 (8/11/2011 Response), 8-9 (comparing claimed and reference concentrations of cationic lipid). This difference across prosecution histories further confirms that claim 1 of the '378 patent does not include a cationic lipid mol % limitation, and the Court should reject Moderna's attempt to import one into the claim.

2. Moderna's Answering Position

Arbutus made a clear and unmistakable disclaimer of lipid particles with less than 50 mol% cationic lipid, and Moderna's construction appropriately holds Arbutus to that disclaimer.

The '378 Patent is the most recent in the Molar Ratio Patent family and recites "a cationic lipid having a protonatable tertiary amine." J.A. 6 ('378 Patent) at claim 1. The '378 Patent was filed only after Moderna had rolled out its COVID-19 vaccine, and is in a long line of continuation applications from the '069 Patent, which was filed in 2009. The '069 Patent was filed and issued with one independent claim, claiming "[a] nucleic acid-lipid participle comprising . . . a cationic

lipid comprising from 50 mol % to 65 mol % of the total lipid present in the particle." J.A. 1 ('069 Patent) at claim 1. All other issued family members prior to the '378 Patent contained similar independent claims, limited to particles with at least 50 mol % cationic lipid. Br. at 49.

While claim 1 of the '378 Patent does not explicitly recite the mol % of the cationic lipid in the lipid particle (as all earlier related patents do), *id.*, Arbutus disclaimed particles with less than 50 mol % cationic lipid during prosecution of the earlier '069 Patent and again in the recent IPR. That disclaimer applies equally to the '378 Patent. When, like here, "the application of prosecution disclaimer involves statements from prosecution of a familial patent relating to the same subject matter as the claim language at issue in the patent being construed, those statements in the familial application are relevant in construing the claims at issue." *Heuft Systemtechnik GMBH v. Indus. Dynamics Co*., 282 F. App'x 836, 841 (Fed. Cir. 2008) (quoting *Ormco Corp. v. Align Tech., Inc.*, 498 F.3d 1307, 1314 (Fed. Cir. 2007)).

a. Arbutus made a clear and unmistakable disclaimer during prosecution of the '069 Patent.

During prosecution of the '069 Patent, the examiner rejected the claims as obvious over MacLachlan, which taught lipid particles comprising about 2 mol % to about 60 mol % cationic lipid. J.A. 58 ('069 P.H. Jul. 30, 2010 Non-Final Rejection) at 4. In response, the applicant distinguished its alleged invention from MacLachlan by explaining that the ***increased percentage of the cationic lipid above 50 mol %*** led to new and unexpected advantages:

> It is clear from the specification that the present invention is based, in part, on the surprising discovery that 1:57 SNALP formulations provide **new and unexpected results** when used for the *in vitro* or *in vivo* delivery of an active agent, such as a therapeutic nucleic acid (e.g., an interfering RNA). More particularly, Applicants have found that SNALP formulations having **increased** amounts of cationic lipid, *e.g.*, one or more cationic lipids comprising from about 50 mol % to about 65 mol % of the total lipid present in the particle, provide **unexpectedly superior advantages** . . .

J.A. 8 ('069 P.H. Jan. 31, 2011 Resp.) at 9 (emphasis in original); *see also id.* at 9–11. Following

another rejection by the examiner (J.A. 9 ('069 P.H. (May 12, 2011 Non-Final Rejection) at 2-4) the applicant continued to emphasize that the pending claim "***recites narrow ranges*** for each of the lipid components compared to the substantially broader ranges taught by MacLachlan." J.A. 10 ('069 P.H. Aug. 11, 2011 Response) at 8. Even Plaintiffs acknowledge this disclaimer. Br. at 50–51. The '069 Patent thus issued because the applicant narrowly claimed ranges of cationic lipids above 50 mol % to overcome the prior art, thereby disclaiming any range below 50 mol %.

Even more recently, in appealing the PTAB's final written decision of the '435 IPR, Arbutus again characterized the invention narrowly, as being "directed to the ***surprising discovery*** that nucleic acid-lipid particles with high levels of cationic lipids" exhibit "favorable" properties, defining "high levels of cationic lipid" as "50–85 mol%." J.A. 72 ('435 Appeal, D.I. 67) at 19; J.A. 65 ('069 IPR, Paper 15) at 7; J.A. 67 ('069 IPR, Ex. 2004) at 71.

b. That disclaimer also applies to the '378 Patent because it claims the same subject matter and was never rescinded.

Despite its previous disclaimers, Arbutus appears to have subtly omitted an explicit lower limit of cationic lipids in the '378 Patent as part of a prosecution strategy to make it less apparent to the Patent Office that Arbutus was seeking ratios of cationic lipid precluded by the prior art. The timing of the '378 Patent's filing is telling. The application that led to the '378 Patent was filed in April 2021, only ***after*** Moderna's COVID-19 vaccine was approved and rolled out. But Arbutus's ploy does not change the fact that Arbutus disclaimed ranges below 50 mol% and cannot recapture that disclaimed scope in a later related patent. The Federal Circuit confirmed that disclaimer during the prosecution of a parent application applies to related child patents. *Heuft*, 282 F. App'x at 840–41. In *Heuft*, the patentee disclaimed an arrangement with an exit angle less than 30° during prosecution of the parent application, narrowing the claims to an exit angle between 30° to 100°. *Id.* Even though the divisional patent's claims did not include exit angle

ranges, the Federal Circuit found the disclaimer in the parent application of angles below 30° applied to the divisional because it "related to the same subject matter that is at issue in the relevant claim limitations" of the divisional patent. *Id.* at 842. The same logic applies here.

Heuft is not an outlier. Many other courts have similarly found disclaimer applied, even where the child application omits the limitation relied upon in the parent. *See Ormco Corp. v. Align Tech., Inc.*, 498 F.3d 1307, 1314 (Fed. Cir. 2007) ("[P]rosecution disclaimer may arise from disavowals made during the prosecution of ancestor patent applications. When the application of prosecution disclaimer involves statements from prosecution of a familial patent relating to the same subject matter as the claim language at issue in the patent being construed, those statements in the familial application are relevant in construing the claims at issue.") (internal citation and quotation omitted); *see also Integra LifeSciences Corp. v. HyperBranch Med. Tech., Inc.*, C.A. No. 15-819, 2017 WL 3336274, at *11 (D. Del. July 27, 2017) (holding prosecution disclaimer applied to related patents where claims were narrowed during prosecution of a parent application to avoid prior art cited by the examiner, finding the "prosecution history for each of the three relevant patents here demonstrates that when the patentees recited 'visualization agent" (even in claims that did not otherwise include the express 'detectable to a human eye' language), they were indicating that such an agent must be 'detectable to a human eye'"), *report and recommendation adopted*, 2017 WL 5172396 (D. Del. Nov. 8, 2017); *see also Icon Health & Fitness, Inc. v. Hoist Fitness Sys., Inc.*, No. 1:10-cv-193, 2015 WL 4077739, at *11 (D. Utah July 6, 2015) (finding disclaimer applied to a child patent where during prosecution of the parent the applicant amended the claims to include express limitations, even though that limitation was absent in the child application because applicant failed "to alert the examiner that the prior art may need to be re-visited" due to the broadened claims).

Plaintiffs claim that the examiner "understood claim 1 [of the '378 Patent] not to require a particular mol % of cationic lipid." Br. at 51. But Plaintiffs provide no support for this claim, nor could they. Plaintiffs could not have broadened the '378 Patent claims below 50 mol% cationic lipid unless the examiner was notified that the prior disclaimer was withdrawn. *See Hakim v. Cannon Avent Grp.*, 479 F.3d 1313, 1318 (Fed. Cir. 2007) ("Although a disclaimer made during prosecution can be rescinded, permitting recapture of the disclaimed scope, the prosecution history must be sufficiently clear to inform the examiner that the previous disclaimer, and the prior art that it was made to avoid, may need to be re-visited."). No such notice was provided to the examiner during prosecution.[27]

c. The narrow description of the alleged invention in the specification confirms the claims are limited to compositions with at least 50 mol% cationic lipids.

The specification and claims of the Molar Ratio Patents are consistent with Plaintiffs' disclaimer. ***Nowhere*** in the Molar Ratio Patents' specification is there an embodiment of a lipid particle comprising less than 50 mol % of a cationic lipid.[28] To the contrary, the specification provides at least ***70*** embodiments with at 50 mol % or greater of cationic lipid (J.A. 6 ('378 Patent) at 19:22–57; 51:22–28)—a fact even Plaintiffs acknowledge (Br. at 50). The lack of such examples and embodiments make sense—all Molar Ratio Patents share the same specification, characterizing "***[t]he present invention***" as being based on "***the surprising discovery that lipid***

[27] Because this disclaimer was used to avoid prior art, any embodiments in the specification that are already disclosed in the prior art cannot be evidence of a broader claim range as Plaintiffs suggest. For example, whether the "specification discloses embodiments with a noncationic lipid (*e.g.*, phospholipid and cholesterol) of greater than 50 mol %" (Br. at 50) does not permit Plaintiffs the ability to expand claimed ranges already disclaimed. *See Rheox*, 276 F.3d at 1326–27; *see also Revolution Eyewear*, 175 F. App'x at 356.

[28] Tables 2 and 4 contain examples with cationic lipid below 50 mol %, but the patent presents those as prior art to show that the 1:57 SNALP formulation, with 57.1 mol % cationic lipid, is the embodiment of the invention. J.A. 1 ('069 Patent) at 70:20–23, 72:21–23, Table 2 and 4.

particles comprising ***from about 50 mol %*** to about 85 % of a cationic lipid . . . ***provid[ed] advantages*** . . . " J.A. 6 ('378 Patent) at 6:6–13; J.A. 1 ('069 Patent) at 5:44–51. *See Heuft*, 282 F. App'x at 842; *see also Irdeto Access, Inc. v. Echostar Satellite Corp.*, 383 F.3d 1295, 1300 (Fed. Cir. 2004) ("while the specification does not contain any statements of explicit disavowal or words of manifest exclusion, it repeatedly, consistently, and exclusively uses exclusively uses "group" to denote fewer than all subscribers, manifesting the patentee's clear intent to so limit the term").

Contrary to Plaintiffs' argument, Moderna's construction does not re-write the claims; rather, Moderna's construction merely holds Plaintiffs to their explicit disclaimer that was never withdrawn. Plaintiffs rely on *H-W Technology*, *Arlington Industries*, and *EIS*, but ***none*** involved disclaimer for the term at issue (Br. at 49). *H-W Tech., L.C. v. Overstock.com, Inc.*, 758 F.3d 1329 at 1333 (Fed. Cir. 2014) (affirming decision not to correct an error in a claim); *Arlington Indus., Inc. v. Bridgeport Fittings, Inc.*, 632 F.3d 1246 at 1255 (Fed. Cir. 2011) ("split"); *EIS, Inc. v. IntiHealth Ger GmbH*, No. 19-1227, 2023 WL 346631, at *3 (D. Del. Jan. 9, 2023) ("connection element"). Plaintiffs' argument that Moderna's construction would "truncate" the upper limit of the phospholipid/cholesterol range is also unavailing. Br. at 49. Indeed, each of the other Molar Ratio Patents include the same purported problem. *See, e.g.*, J.A. 1 ('069 Patent) at claim 1 (where 65 mol % cationic lipid and 40 mol % non-cationic lipid exceed 100%); J.A. 2 ('359 Patent) at claim 1 (same); J.A. 3 ('668 Patent) at claim 1 (where 85 mol % cationic lipid and 49.5 mol % non-cationic lipid exceed 100%).

Consistent with Plaintiffs' clear disclaimer, claim 1 of the '378 Patent should be construed to comprise "a cationic lipid having a protonatable tertiary amine comprising 50 mol % or more of the total lipid present in the finished lipid particle."

3. Plaintiffs' Reply Position

Moderna acknowledges that the '378 patent claims lack any limitation on the percentage

of cationic lipid. That ends the inquiry. The Federal Circuit "repeatedly and consistently has recognized that courts may not redraft claims," as Moderna urges. *Rembrandt Data Techs., LP v. AOL, LLC,* 641 F.3d 1331, 1339 (Fed. Cir. 2011).

Notwithstanding this precedent, Moderna asks the Court to ignore the plain language because—yet again—Plaintiffs supposedly made a "clear and unmistakable" disavowal of cationic lipid percentages outside the range Moderna seeks to write into the claims. Br. 52. This attempt fails for many reasons. Moderna does not argue that the specification contains the requisite "words or expressions of manifest exclusion." *Unwired Planet*, 829 F.3d, 1358; Br. 55-56. Indeed, Moderna concedes that the specification discloses embodiments with greater than 50 mol % noncationic lipid, in which the cationic lipid must be less than 50 mol %. Br. 49-50; Br. 55 n.27. Contra Moderna (Br. 55-56), black-letter law holds that the specification's disclosure of other embodiments with more than 50 mol % cationic lipid does not limit the claims. Br. 49-50; *Martek*, 579 F.3d at 1381. Nor does the specification's disclosure about the "present invention" and its advantages, Br. 55-56, especially given its clarifying language—omitted conspicuously by Moderna—that the "present invention is based, ***in part***, upon the surprising discovery" regarding various lipid ranges, confirming that those ranges and advantages are just one aspect of the invention. '378 patent, 6:6-13. The remainder of the specification is in accord. Br. 49-50.

Unable to find any disavowal in the specification or file history of the '378 patent, Moderna turns instead to statements from the prosecution of ***parent*** applications. In particular, Moderna cites two statements related to the "advantages" of the amounts of cationic lipid explicitly claimed in the parent '069 and '435 patents. Br. 52-53. The Federal Circuit, however, repeatedly has rejected Moderna's argument that such advantages should be read into the claims. *Phillips*, 415 F.3d at 1327; *Golight, Inc. v. Wal-Mart Stores, Inc*., 355 F.3d 1327, 1331 (Fed. Cir. 2004) (each

claim is not required to include all "advantages or features described as significant or important"); *Yoon Ja Kim v. ConAgra Foods, Inc.*, 465 F.3d 1312, 1319 (Fed. Cir. 2006). Moderna also cites a statement from the '069 file history comparing the "narrow ranges" of the claimed lipid components to the disclosures in the cited reference. Br. 53 (quoting J.A. 10). That discussion, however, distinguished the reference based on the overall narrowness of the claimed lipid ranges, not the 50 mol % cationic lipid value specifically. J.A. 10 (8/11/2011 Response), 8.

More fundamentally, the claims at issue during prosecution of the parent applications differed in a relevant and critical way from the asserted '378 patent claims: they included explicit limitations requiring particular amounts of cationic lipid. *E.g.*, '069 patent, claim 1 ("a cationic lipid comprising from 50 mol % to 65 mol % of the total lipid present in the particle"). The asserted claims of the '378 patent do not. The Federal Circuit consistently has refused to apply prosecution disclaimers directed to particular claim terms that are omitted from subsequent applications. *E.g.*, *Sanofi v. Watson Labs. Inc.*, 875 F.3d 636, 650 (Fed. Cir. 2017) (disclaimer of polysorbate surfactants in parent did not apply in child not containing the same limitation); *Regents v. AGA Medical Corp.*, 717 F.3d 929, 943 (Fed. Cir. 2013) ("a prosecution disclaimer will only apply to a subsequent patent if that patent contains the same claim limitation as its predecessor"); *Saunders Grp., Inc. v. Comfortrac, Inc.*, 492 F.3d 1326, 1333 (Fed. Cir. 2007) ("When the purported disclaimers are directed to specific claim terms that have been omitted or materially altered in subsequent applications (rather than to the invention itself), those disclaimers do not apply.").

Ignoring this controlling precedent, Moderna features a non-precedential case, *Heuft*. Br. 53-54. Even were it binding, *Heuft* is readily distinguishable. It involved disclaiming arguments regarding the exit angle that were made even when "no independent claim contained a limitation relating to the exit angle." 282 F. App'x 836, 839 (Fed. Cir. 2008). The evidence in *Heuft* was

that the disclaimer went to the invention as a whole, rather than a particular limitation. *E.g.*, *id.* at 840 (applicant sought to amend the ***specification*** to describe angle as the "critical feature" of the invention). Courts in this District have declined to follow *Heuft* on these and other grounds.[29] *E.g.*, *Sanofi v. Glenmark Pharms. Inc., USA*, 204 F. Supp. 3d 665, 702-04 (D. Del. 2016); *Broadridge Fin. Sols., Inc. v. Inveshare, Inc.*, 2012 WL 1245723, at *4-5 (D. Del. Apr. 11, 2012).

Moderna fails to cite ***any*** evidence of disavowal from the prosecution of the '378 patent itself. Instead, Moderna contends that Arbutus "subtly omitted" the limitation related to the amount of cationic lipid and—citing *Hakim*—argues that Arbutus was obliged to notify the Examiner "that the prior disclaimer was withdrawn." Br. 53. As explained above, there was no disclaimer to withdraw. In any event, Moderna fails to explain what was "subtle" about the clear omission of the cationic lipid amount limitation. The law does not require any additional notification when an applicant prosecutes a plainly broader continuation application. *E.g.*, *Sanofi*, 875 F.3d at 650 (continuations with "claims that lack the narrowing limitation" are a "familiar pattern"; rejecting disclaimer); *Middleton, Inc. v. Minnesota Mining & Mfg. Co.*, 311 F.3d 1384, 1389 (Fed. Cir. 2002) (rejecting disclaimer argument in "a continuation that broadened the invention"); *Warner Chilcott Co., LLC v. Amneal Pharms., LLC*, 2014 WL 1391536, at *7 (D.N.J. Apr. 9, 2014) (distinguishing *Hakim* because "the patentee changed more than a modifier, omitting a claim limitation entirely"). Moreover, Moderna entirely ignores evidence from the '378 patent's

[29] The other cases Moderna cites, Br. 54, are also distinguishable. In *Ormco*, the specification indicated disavowal; the disavowal-related prosecution statements were "not associated with particular [claim] language"; and there was no omission of a limitation that gave rise to disavowal. 498 F.3d at 1313-15. In *Integra*, all of the claims included the term giving rise to disavowal ("visualization agent"), and the applicant made disavowal-related arguments both for claims that did and did not contain the "detectable to a human eye" language. 2017 WL 3336274, at *9-11. In *Icon Health*, the disclaimer applied to a continuation application because it "used the same claim terms (namely, offset and parallel axes of rotation)" "to which the disclaimer attached." 2015 WL 4077739, at *10-11. By contrast, the percent cationic lipid limitation is absent in the '378 patent.

file history, Br. 50-51, demonstrating that both the applicant and Examiner understood the claims ***not*** to require a mol % of cationic lipid.[30] *See* J.A. 13 (6/14/2021 Non-Final Rejection), 3-6 (citing art for cationic lipid limitation, but not percentage above 50). Courts have found *Hakim* inapplicable in similar situations. *E.g.*, *Amgen Inc. v. Mylan Inc.*, 2018 WL 6061213, at *13 (W.D. Pa. Nov. 20, 2018) ("Unlike in *Hakim*, the examiner evaluated and considered arguments for a broader claim scope rather than issuing the claims without comment."); *Sanofi*, 204 F. Supp. 3d at 704 ("The extensive prosecution history of the '800 patent also demonstrates the examiner's awareness that the applicant intended to capture polysorbates within the claims and therefore satisfies the concern raised in *Hakim* that, without additional prosecution, the claims may have been allowed based on the prosecution history of the parent patent.").

At bottom, Moderna argues that the Examiner conducted substantial examination of claims without recognizing that they lacked a cationic lipid range; the law presumes, and the file history unmistakably shows, otherwise. *Brooktree Corp. v. Adv. Micro Devices, Inc.*, 977 F.2d 1555, 1574-75 (Fed. Cir. 1993) ("patent examiners [are] presumed to have done their job").

4. Moderna's Sur-reply Position

Moderna's construction does not rewrite the claims but merely holds Plaintiffs to their disclaimer. Plaintiffs' handwaving regarding the '378 patent claims' lack of a percentage of cationic lipid is unavailing in light of Federal Circuit precedent establishing that "statements from prosecution of a familial patent relating to the ***same subject matter*** as the claim language at issue . . . are relevant in construing the claims at issue." *Ormco*, 498 F.3d at 1314.

[30] Moderna concedes that its reading truncates the combined phospholipid/cholesterol range of claim 1. Br. 49; Br. 56. Moderna is wrong that this same problem applies to other patents in the family, in which the full scope of each lipid limitation can be practiced by choosing an appropriate amount of the other lipids within their claimed ranges. Under Moderna's construction, the full scope of the claims' combined phospholipid/cholesterol range necessarily cannot be practiced.

Plaintiffs do not dispute that where a patentee "repeatedly, consistently, and exclusively uses" a claim term in a particular manner, the patentee has manifested a clear intent to so limit the term even if the "specification does not contain any statements of explicit disavowal or words of manifest exclusion." *Irdeto*, 383 F.3d at 1303; Br. at 56. This is true here where the specification provides at least ***70 embodiments*** with 50 mol % or greater of a cationic lipid. J.A. 6 at 19:22–57, 51:22–28. There is ***no*** embodiment comprising less than 50 mol % of a cationic lipid. Br. at 55.[31]

Likewise, Plaintiffs concede that Arbutus distinguished the MacLachlan prior-art reference by exclusively relying on the disclosed 1:57 formulation (containing ***more than 50% cationic lipid***). J.A. 8 at 8–10 ("1:57 SNALP formulations provide ***new and unexpected results***"; "**increased** amounts of cationic lipid, *e.g.*, one or more cationic lipids comprising from about 50 mol % to about 65 mol %") (emphases in original). Plaintiffs attempt to characterize this disclaimer as a purported advantage of the claims. Not so. The ranges are not mere advantages—they are the claimed invention in each of the Molar Ratio Patents. *E.g.*, '069 patent, claim 1, '378 patent, claim 1; *see also* J.A. 8 at 10 (referring to the 1:57 SNALP formulation as the "presently claimed" formulation); J.A. 11. In fact, Arbutus continued to rely on this distinction that the "present invention is based, in part, upon the ***surprising discovery*** that lipid particles comprising from about ***50 mol %*** to about 85 mol % of a cationic lipid" after prosecution of the '069 patent. J.A. 6 at 6:6–13; *see also* J.A. 72 at 19; J.A. 65 at 7; J.A. 67 at ¶ 168.

Plaintiffs further agree that "the claims at issue during prosecution of the parent applications differed in a relevant and critical way from the asserted '378 patent claims: they

[31] Moderna did not concede that the specification includes embodiments with <50 mol% cationic lipid. Br. at 57. Rather, Moderna stated that "whether [or not] the specification discloses [such] embodiments" does not permit Plaintiffs to expand claimed ranges already disclaimed. *See* Br. at 55 n.27 (citing *Rheox*, 276 F.3d at 1326–27). Plaintiffs do not address, and thus concede, this point.

included explicit limitations requiring particular amounts of cationic lipid." Br. at 58. But Plaintiffs gloss over the fact that the claims in the other Molar Ratio Patents were allowed because Arbutus had earlier disclaimed broader ranges during prosecution of the '069 patent in favor of "narrower ranges." J.A. 10 at 8. Plaintiffs even admit that "the '069 file history compar[ed] the 'narrow ranges' of the claimed lipid components to the disclosures in the cited reference." Br. at 58. The claimed cationic lipid is one of these components, and Arbutus should be held to its prior statements differentiating its purported invention from the prior art.

Plaintiffs' case law is inapposite because it only addresses the situation where "claim terms [] are ***omitted*** from subsequent applications," which does not apply here. Br. at 58. The cationic lipid is claimed ***in all*** Molar Ratio Patents. Br. at 52. Indeed, *Regents* explains that disclaimer applies when "two patents [] have ***the same or closely related claim limitation*** language," as is the case here. 717 F.3d at 943. In *Saunders*, the embodiment in question was not "an essential component of the invention." 492 F.3d at 1333. Here, the patent, file history, and IPRs all express the importance of the claimed cationic ranges.[32] *See* J.A. 6 at 6:6–13; J.A. 8 at 9; J.A. 72 at 19; J.A. 65 at 7; J.A. 67 at ¶ 168. *Broadridge* does not apply because the claims in the related patent were materially different from the claim at issue, which Plaintiffs do not argue here. 2012 WL 1245723, at *4–*6. Likewise, Plaintiffs' attempt to distinguish *Heuft* fails. Br. at 58–59. Just as in *Heuft*, the disclaimer here goes "to the invention as a whole" (Br. at 59)—the Molar Ratio Patents describe the lipid molar ratios, and specifically the cationic lipid, as the "surprising discovery."[33]

Plaintiffs do not dispute that notice is required when a patentee attempts to withdraw a disclaimer but disagree that there was disclaimer here. Br. at 59–60. As explained above,

[32] Plaintiffs agree. Br. at 58 (distinguishing based on "overall narrowness" of the lipid ranges).
[33] *Sanofi* distinguishes *Heuft* because the claim amendment in *Heuft* involved "critical features of the invention," as it does in the '378 Patent. 204 F. Supp. 3d at 702–04 (internal citation omitted).

disclaimer applies. Therefore, Plaintiffs' case law regarding the broadening of claims is inapplicable. For example, in *Middleton*, the parent patent "claimed only bowling alleys and bowling alley surfaces." 311 F.3d at 1388. After rejection, the applicant amended his claims and distinguished certain prior art related to the uniformity of "smooth ***sporting*** surfaces." *Id.* at 1389. The Federal Circuit unremarkably found that the prosecution history "does not limit the broader claims to other flooring surfaces." *Id.* Unlike *Middleton*, the disclaimer here is directed to the ***same*** subject matter—the cationic lipid in a lipid particle. *Warner* does not apply for the same reason. 2014 WL 1391536, at *7 (finding the "subject matter of the claims [] differ"). Indeed, *Amgen* confirms that "[d]isclaimers made during the prosecution of parent patent applications can apply to later-filed child applications, even if the child applications are filed with broader claims." 2018 WL 6061213, at *12–13 (declining to apply *Hakim* where examiner re-reviewed prior art evaluated during prosecution of parent). Here, the Examiner did not reevaluate the reference that led to the rejection and Arbutus's disclaimer. J.A. 13. Arbutus could have provided the Examiner with notice that it was withdrawing its disclaimer but chose not to. This Court should not permit Plaintiffs to recapture previously disclaimed scope. *Hakim*, 479 F.3d at 1318.

C. "wherein at least 70% / at least 80% / about 90% of the mRNA in the formulation is fully encapsulated in the lipid vesicles" / "fully encapsulated"

Plaintiffs' Proposed Construction	Moderna's Proposed Construction
"wherein at least 70% / at least 80% / about 90% of the mRNA in the formulation is contained inside the lipid vesicles"	"fully, as distinct from partially, encapsulated" "wherein at least 70% [/ 80% / 90%] of the mRNA in the formulation is fully, as distinct from partially, encapsulated in the lipid vesicles"
'651 Patent, Claims 1, 13, 14	

1. Plaintiffs' Opening Position

U.S. Patent No. 9,504,651 (the "'651 patent") claims novel lipid vesicles with certain lipid

components and mRNA. The inventors discovered new ways to synthesize these vesicles, including with a device called a "T-connector." *See* '651 patent, Figure 13. These methods yielded vesicles with beneficial properties, including the ability to encapsulate a surprisingly high percentage of the nucleic acid inside vesicles, thereby protecting the nucleic acid from degradation when the vesicles are administered to patients. *Id.*, 15:19-56, 18:30-43. The '651 patent claims particular lipid compositions with those improved properties. *See* J.A. 7 (Thompson) ¶¶ 29-31.

The sole dispute concerning the '651 patent arises from Moderna's effort to strip the term "fully encapsulated" from its context in the claim and then import language from the specification to construe it. Moderna does not offer its construction to aid the jury in understanding the claim scope; in fact, Moderna intends to argue that ***its own construction***—"fully, as distinct from partially, encapsulated"— is indefinite. D.I. 129 at 2. Moderna's construction ignores the context of the claim and the purpose of this limitation. The POSA would have understood that the full claim term at issue delineates (1) the proportion of mRNA in the lipid vesicles (at least 70% / 80% or about 90%), and (2) the location of the mRNA, which is contained ***inside*** the vesicles. J.A. 7 (Thompson) ¶ 73. Plaintiffs' proposed construction accurately captures these concepts reflected in the intrinsic record, whereas Moderna's proposed construction flouts them.

With respect to the first issue, the POSA would have recognized that the limitation as a whole refers to the proportion of mRNA that is encapsulated by lipid vesicles, as reflected in Plaintiffs' proposed construction. J.A. 7 (Thompson) ¶ 74. That measurement—commonly known as "encapsulation efficiency"—can be made by the POSA using a fluorescent dye that binds to nucleic acid. *Id.* ¶ 91. That dye is lipid impermeable—it cannot pass through lipids—and thus it cannot access, interact with, or detect nucleic acid encapsulated by the lipids. *Id.* Subsequently in the measurement technique, the POSA adds a detergent to break down the lipid

barrier, which releases the nucleic acid previously encapsulated by the lipids (which the dye, before detergent was added, could not reach). *Id.* The POSA then measures fluorescence again, to ascertain the total amount of nucleic acid (nucleic acid the dye could not reach before detergent was added plus nucleic acid the dye could reach before the detergent was added). *Id.* From these values, the POSA can calculate the percentage of nucleic acid that was encapsulated. *Id.*

Extensive intrinsic evidence confirms Plaintiffs' position. The inventors of the '651 patent achieved surprisingly high encapsulation efficiencies, as the specification confirms. The specification repeatedly reports the favorable encapsulation efficiencies the inventors achieved, including the very encapsulation percentages recited in the claims. *See, e.g.*, '651 patent 2:51-54 ("encapsulation efficiency is as high as about 90%"), 8:7-11 (the disclosure "herein provides for encapsulation of therapeutic agent in the formed liposome . . . with an encapsulation efficiency of up to about 90%"), 9:24-26, 36-38 (disclosing 70-80% of "therapeutic agent entrapment"), 12:63-13:2 ("the processes and apparatus of the present invention provide an encapsulation efficiency . . . of up to about 90%"), 15:32-33, 18:40-42, Figures 5-8 (showing measured encapsulation efficiencies of at least 70%, at least 80%, and up to about 90%). These encapsulation efficiencies from the specification match the encapsulation values of "at least 70%," "at least 80%," and "about 90%" recited in the claims and thereby inform their meaning. '651 patent, claims 1, 13, 14. The specification is clear to the POSA that the specification's disclosed encapsulation efficiencies correspond to the fully encapsulated percentages recited in the claims. J.A. 7 (Thompson) ¶¶ 78-81; *Phillips*, 415 F.3d at 1316 ("construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be, in the end, the correct construction").

The file history provides further support for Plaintiffs' construction by demonstrating that

both the Examiner and applicant understood the meaning of fully encapsulated consistent with Plaintiffs' construction. The percent fully encapsulated limitations were added to overcome an obviousness rejection over WO 98/51278 ("Semple"), which the Examiner had argued disclosed lipid particles with encapsulation efficiencies in excess of 50%. *See* J.A. 21 (8/18/2015 Response), 8 ("[T]he Examiner notes that this feature of encapsulation efficiency is not recited in the rejected claims. In an earnest effort to advance prosecution, but without acquiescing on the merits of the present rejections, Applicants have amended claim 1 to recite a lipid vesicle formulation wherein at least 50% of the mRNA in the formulation is fully encapsulated in the lipid vesicles."). In response, the applicant noted that, by requiring a percentage of "fully encapsulated mRNA" in the claims, "the very low encapsulation efficiency associated with the method described in Semple *et al.* is well below ***the minimum mRNA encapsulation efficiency required in the presently claimed formulations***." *Id.*; *id.* at 9 (discussing the "mRNA encapsulation efficiency as presently claimed"). The applicant also submitted declarations during prosecution explicitly equating the percent "fully encapsulated" claim limitation with encapsulation efficiency measurements. J.A. 23 (12/14/2015 Decl.) ¶ 15 ("lipid vesicles with an ***mRNA encapsulation efficiency as presently claimed***"); J.A. 25 (5/19/2016 Decl.) ¶¶ 7, 12, 13 (same). These statements reflect that the percent fully encapsulated limitations refer to encapsulation efficiency, and the Court should construe the claims accordingly. *Arlington Indus.*, 632 F.3d at 1255; *Phillips*, 415 F.3d at 1317; J.A. 7 (Thompson) ¶¶ 82-90.

The Examiner likewise equated disclosures of encapsulation efficiency with the percent fully encapsulated limitations. The Examiner rejected the application as obvious over U.S. Patent No. 6,734,171 ("Saravolac"), which, the Examiner argued, disclosed lipid vesicles "wherein the encapsulation efficiency of the mRNA in the vesicles is about 80% and can even approach 90%

which ***reads upon the instantly claimed at least 70%, more specifically at least 80%, and about 90%.***" J.A. 22 (10/9/2015 Non-Final Rejection), 7. The applicant responded with encapsulation efficiency measurements obtained using Saravolac's particle formation process. J.A. 23 (12/14/2015 Response & Decl.); J.A. 24 (4/15/2016 Rejection); J.A. 25 (5/19/2016 Response & Decl.). Relying on these measurements, the Examiner found that "Saravolac does not encapsulate mRNA with the efficiency that is instantly claimed in their lipid vesicles." J.A. 26 (10/3/2016 Rejection), 6. This consistent understanding of the claim term by both the applicant and the Examiner further confirms that Plaintiffs' construction is correct. *See Phillips*, 415 F.3d at 1317; J.A. 7 (Thompson) ¶¶ 82-90.

With respect to the second issue—the location of the mRNA—the POSA would have recognized that "fully encapsulated" refers to the mRNA being ***contained inside*** the vesicle. *See* J.A. 7 (Thompson) ¶ 92. Consistent with the understanding in the field, the specification describes lipid systems where the nucleic acid is in different locations. In some, such as liposome complexes (*i.e.*, "lipoplexes") or lipid aggregates, the nucleic acid is part of "a relatively disordered lipid mixture"—akin to, for example, spaghetti (nucleic acid) surrounded by meatballs (lipids). '651 patent, 5:35-37; *see* J.A. 7 (Thompson) ¶¶ 19, 93; J.A. 34, 364 (Figure 2). Alternatively, the nucleic acid can be on the "interior"—that is, contained ***inside***—the vesicles. '651 patent, 5:30-35, 5:41-45; J.A. 7 (Thompson) ¶ 93; J.A. 31 (MacLachlan 2007), 239 ("[I]t is important to distinguish first-generation 'lipoplex' or 'oligoplex' systems from those that truly encapsulate their NA payload."). The specification further characterizes these distinct lipid systems, where the nucleic acid is in different locations, as representing "partial encapsulation" or "full encapsulation." '651 patent, 5:38-40. The claims are directed to systems where the mRNA is in the interior, contained inside the vesicle, not merely part of "a relatively disordered lipid mixture."

Compare '651 patent, 5:30-35, *with* 5:35-37; *see* J.A. 7 (Thompson) ¶¶ 92, 99; J.A. 31 (MacLachlan 2007), 239; J.A. 19 (5/12/2015 Response), 6-8.

The prosecution history confirms that "fully encapsulated" refers to the location of the nucleic acid. The Examiner initially rejected the claims, including the "fully encapsulated" language, over the Unger reference. J.A. 18 (2/13/2015 Non-Final Rejection), 10. The applicant explained that Unger used lipoplexes, "in which little, if any, of the DNA payload is encapsulated ***within*** the preformed cationic liposomes," and instead "is merely ***associated with the surface*** of the preformed liposome." J.A. 16 (10/22/2014 Response), 7. Unger thereby differed from "the encapsulated mRNA present ***within the lipid vesicles*** of the present invention." *Id.* And the applicant concurrently submitted a declaration that drew the same distinction. J.A. 16 (10/22/2014 Decl.) ¶ 10.

Moderna proposes to construe the isolated phrase "fully encapsulated" to mean "fully, as distinct from partially, encapsulated." Moderna draws its construction from the patent's definition of a ***different term***: "lipid encapsulated." '651 patent 5:38-40 ("'lipid encapsulated' can refer to a lipid formulation which provides a compound with full encapsulation, partial encapsulation, or both"). That definition accords with Plaintiffs' construction: nucleic acid is "lipid encapsulated" when it is contained inside vesicles ***or*** when it is part of a "disordered lipid mixture," '651 patent, 5:30-37, but the mRNA is only "fully encapsulated" (as set forth in the claims) when it is contained inside the vesicles. J.A. 7 (Thompson) ¶ 94. In any event, while "claims are interpreted in light of the specification[, that] does not mean that everything expressed in the specification must be read into the claims." *Raytheon Co., v. Roper Corp.,* 724 F.2d 951, 957 (Fed Cir. 1983). A definition controls only when it "clearly set[s] forth a definition of the disputed claim term." *Cont'l Circuits LLC v. Intel Corp.,* 915 F.3d 788, 796 (2019). Here, the word "partial" only appears in a

definition of a different term ("lipid encapsulated"). This disclosure is not properly read into the claims. *Raytheon*, 724 F.2d at 957.

By its own admission, Moderna's proposed construction would not clarify the claim scope for the jury. Instead, Moderna urges a "construction" in an effort to manufacture a future invalidity argument. Specifically, and remarkably, Moderna clarified during the parties' meet-and-confers—and in the Joint Claim Construction Chart, D.I. 129 at 2—that it intends to argue that the claims are indefinite ***under Moderna's own proposed construction***. Moderna's error results, in part, from its effort to construe only part of the claim limitation and thereby manufacture ambiguity where none exists. *See Phillips*, 415 F.3d at 1314 ("the context in which a term is used in the asserted claim can be highly instructive"). Declining to construe "fully encapsulated" in conformity with the percentage encapsulation language that precedes it, Moderna asserts that because "fully encapsulated" cannot mean 100% encapsulation efficiency (because the claim recites percentages below 100), the POSA could not understand what it means. J.A. 30 (Invalidity Contentions), 137. To the contrary, the POSA would understand that the limitation as a whole works together—the percentage refers to the encapsulation efficiency, and "fully" refers to the location of the mRNA. Moderna's gamesmanship defies the purpose of claim construction—that is, to "determine the meaning and scope of the patent claims," *O2 Micro Intern. Ltd. v. Beyond Innovation Tech. Co.*, 521 F.3d 1351, 1360 (Fed. Cir. 2008)—and violates the canon that "courts should attempt to construe claims to preserve their validity." *Omega Engineering, Inc, v. Raytek Corp.*, 334 F.3d 1314, 1335-36 & n.6 (Fed. Cir. 2003) (reversing construction that would render claims indefinite). Accordingly, the Court should adopt Plaintiffs' proposed construction.

2. Moderna's Answering Position

As shown below, the '651 Patent claims a "lipid vesicle formulation" comprising lipid vesicles with three to four lipids and mRNA, wherein at least a certain percentage "of the mRNA

in the formulation is ***fully encapsulated*** in the lipid vesicles:"

1. A lipid vesicle formulation comprising:
(a) a plurality of lipid vesicles, wherein each lipid vesicle comprises:
a cationic lipid;
an amphipathic lipid; and
a polyethyleneglycol (PEG)-lipid; and
(b) messenger RNA (mRNA), wherein at least 70% of the mRNA in the formulation is fully encapsulated in the lipid vesicles.

13. The lipid vesicle formulation of claim **1**, wherein at least 80% of the mRNA in the formulation is fully encapsulated in the lipid vesicles.

14. The lipid vesicle formulation of claim **1**, wherein about 90% of the mRNA in the formulation is fully encapsulated in the lipid vesicles.

J.A. 5 ('651 Patent) at Claims 1, 13, 14. Based on the inventors' express definition of "lipid encapsulated" distinguishing between "full encapsulation" and "partial encapsulation," here, "fully encapsulated" must mean "fully, as opposed to partially encapsulated," as Moderna proposes. Plaintiffs ignore the word "fully" and seek to mask the proper construction by requesting construction of additional claim language that is not disputed.

a. The inventors defined "lipid encapsulated" to distinguish between "fully encapsulated" and "partially encapsulated."

The parties agree that "fully" encapsulated does not refer to the ***amount*** of encapsulated mRNA because the amount is recited by percentage. Instead, "fully" must define a separate characteristic, such as the state or location of the encapsulated mRNA. Br. at 64, 67–68.

The specification defines "lipid encapsulated" by contrasting two separate concepts: "full encapsulation" and "partial encapsulation" (J.A. 5 ('651 Patent) at 5:38–40):

> As used herein, "lipid encapsulated" can refer to a lipid formulation which provides a compound with full encapsulation, partial encapsulation, or both.

This is the only place in the specification where "full" is used in connection with "encapsulation." The inventors' choice to define "lipid encapsulated" by referring to "full" and "partial" encapsulation as alternatives (using "or") confirms that "fully encapsulated" is distinct from

"partially encapsulated."[34] *See Tubular Rollers, LLC v. Maximus Oilfield Prods*., *LLC*, No. 2021-2319, 2023 WL 4230371, at *4 (Fed. Cir. June 28, 2023) ("The use of the 'disjunctive ("or") as the coordinating conjunction' here 'reveals the relationship' between collinear and parallel as 'alternatives,' not as one being a subset of the other."); *see also SkinMedica, Inc. v. Histogen Inc*., 727 F.3d 1187, 1199 (Fed. Cir. 2013) (finding the specification differentiated between alternatives where patentee "use[d] a disjunctive ('or')").

Contrary to Plaintiffs' argument, Moderna's construction does not read "everything expressed in the specification" into the claims. Br. at 68–69. Instead, Moderna's construction is rooted in the sole definition in the specification. At the very least, the specification defines "fully" encapsulated by implication. *See Irdeto Access, Inc. v. Echostar Satellite Corp.*, 383 F.3d 1295, 1300 (Fed. Cir. 2004) ("Even when guidance is not provided in explicit definitional format, the specification may define claim terms by implication such that the meaning may be found in or ascertained by a reading of the patent documents.") (internal quotations and citations omitted). Moderna's construction aligns with the claim language and the only passage in the specification defining "full" encapsulation as distinct from "partial" encapsulation. *Cf. Helmsderfer v. Bobrick Washroom Equip., Inc.*, 527 F.3d 1379, 1383–84 (Fed. Cir. 2008) (affirming construction of "partially hidden from view" as "hidden from view to some extent but not totally hidden from view," where "the ordinary and customary meaning of the term 'partially' excludes 'totally'").

b. Plaintiffs' construction ignores the word "fully" and the inventors' definition, instead using phrases that are not found in the specification.

Plaintiffs' proposed construction impermissibly completely ignores the claim text of

[34] "Both" in the definition refers to the "formulation" ***containing*** both alternative forms ("full" and "partial"), rather than suggesting a nucleic acid could ***be*** both fully and partially encapsulated.

"fully." This is made clear by the fact that Plaintiffs apparently define the term "encapsulated" no differently then the term "fully encapsulated"—both merely mean "contained within" ***giving absolutely no meaning to the word "fully."*** This is improper because "claims are interpreted with an eye toward giving effect to all terms in the claim." *Bicon, Inc. v. Straumann Co.*, 441 F.3d 945, 950–51 (Fed. Cir. 2006) ("[a]llowing a patentee to argue that physical structures and characteristics specifically described in a claim are merely superfluous would render the scope of the patent ambiguous, leaving examiners and the public to guess about which claim language the drafter deems necessary to his claimed invention and which language is merely superfluous"); *Wasica Fin.*, 853 F.3d at 1288 n.10 (Fed. Cir. 2017) ("It is highly disfavored to construe terms in a way that renders them void, meaningless, or superfluous."); *Texas Instruments Inc. v. U.S. Int'l Trade Comm'n*, 988 F.2d 1165, 1171 (Fed. Cir. 1993) (declining to construe claims to read out an express limitation "because courts can neither broaden nor narrow claims to give the patentee something different than what he has set forth"). In doing so, Plaintiffs do not acknowledge the specification's distinction between "full" and "partial" encapsulation. J.A. 5 ('651 Patent) at 5:38–40. Further, Plaintiffs' proposed construction attempts to define the claim with language ("contained inside") that ***appears nowhere*** in the specification or the file history.

To support their proposed construction, Plaintiffs heavily rely on extrinsic evidence, including opinions from Dr. Thompson, who introduces concepts and methods of measuring encapsulation that are mentioned ***nowhere*** in the '651 Patent. Br. at 64–66; J.A. 7 (Thompson Decl.) ¶¶ 77, 82–83, 91. Where, as here, the specification expressly defines the term, such extrinsic evidence should be disregarded. *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1585 (Fed. Cir. 1996) ("Because the specification clearly and unambiguously defined the disputed term in the claim, reliance on this extrinsic evidence was unnecessary and, hence, legally incorrect.").

c. The inventors did not define "fully encapsulated" as "contained inside" during prosecution.

Plaintiffs argue that the prosecution history supports their construction of "fully encapsulated" as "contained inside," based on statements Arbutus made to overcome the prior art. Br. at 68. But Plaintiffs do not point to any place in the prosecution history where the term "contained inside" is used. *Id*. And, more importantly, Arbutus did not distinguish the prior art based on the lack of "***fully*** encapsulated" nucleic acids; instead it merely distinguished between "encapsulation" and "association" with the liposome. Specifically, Arbutus argued that certain prior art did not teach "the successful ***encapsulation*** and delivery of mRNA," which instead taught nucleic acid "merely ***associated*** with the surface of a preformed liposome." J.A. 16 ('651 P.H., Oct. 22, 2014 Resp.) at 5, 7; *see also* J.A. 19 ('651 P.H., May 12, 2015 Resp.) at 6 (distinguishing prior art complexes with little nucleic encapsulated within liposome); J.A. 7 (Thompson Decl.) ¶¶ 96–97 (summarizing prosecution history). In other words, Arbutus argued that the prior art disclosed nucleic acids that were not encapsulated ***at all*** (either fully or partially), which says nothing about what it means to be "fully encapsulated," let alone defining it as "contained inside."

d. The Court should reject Plaintiffs' attempt to inject method limitations into the '651 Patent's composition claims.

Contrary to Plaintiffs' position (Br. at 64–65),[35] the claim term refers to the percentage of the "mRNA in the formulation" that is "fully encapsulated," not "encapsulation ***efficiency***." "Encapsulation efficiency" is used in the specification to describe ***methods*** of encapsulating nucleic acids, which was specifically claimed in related patents, but not in the '651 Patent. *See, e.g.*, J.A. 53 (U.S. Pat. No. 7,901,708) at claim 5 ("5. The ***process*** of claim 1, wherein the lipid vesicle is in a solution having a pH of about 5 or lower, and wherein said lipid vesicle ***has a nucleic***

[35] Plaintiffs failed to disclose this part of its construction in the Joint Claim Construction Statement, which should be treated as waived. D.I. 129 at 5–9.

acid encapsulation efficiency of between about 80% and about 90%."); *Liqwd, Inc. v. L'Oréal USA, Inc.*, C.A. No. 17-14-JFB-SRF, 2019 WL 1977367, at *3 (D. Del. May 2, 2019) ("Different words in a patent have different meanings and the same words have the same meaning.") *aff'd sub nom*, *Olaplex, Inc. v. L'Oréal USA, Inc.*, 845 F. App'x 943 (Fed. Cir. 2021); *see also Allergan Sales, LLC v. Sandoz., Inc.*, No. 2:12-CV-00207-JRG, 2013 WL 4854786, at *5 (E.D. Tex. Sept. 5, 2013) (rejecting a construction that used a different term in the specification, noting that "[t]he patentees clearly knew how to write the words 'brimonidine tartrate' when they wanted to"). The '651 Patent claims read on any "lipid vesicle formulation" with the recited lipids, as long as "70% of the mRNA ***in the formulation***" is "fully encapsulated." In fact, the claims would cover a formulation made by a process with a poorer encapsulation efficiency (*e.g.*, 30%), if the free and unencapsulated nucleic acid was filtered out as the art taught. *See, e.g.*, J.A. 45 (U.S. Patent No. 6,734,171) at 14:43-45, 15:13-18, 22:11-21. A "method of manufacture, even when cited as advantageous, does not of itself convert product claims into claims limited to a particular process." *Vanguard Prod. Corp. v. Parker Hannifin Corp*., 234 F.3d 1370, 1372 (Fed. Cir. 2000). In short, nothing in the claim requires the percent of "mRNA in the formulation" that is "fully encapsulated" to have been made by a specific process or method, let alone by an efficient one.

e. Plaintiffs' insinuation that Moderna is manufacturing an indefiniteness argument is false.

As discussed above, Moderna's proposed construction is based on the inventors' express definition of "lipid encapsulated"—the only passage where "full" encapsulation is addressed. "[A]rticulat[ing] a definition supported by the specification, however, does not end the inquiry" on indefiniteness. *Halliburton Energy Servs., Inc. v. M-I LLC*, 514 F.3d 1244, 1251 (Fed. Cir. 2008) ("Even if a claim term's definition can be reduced to words, the claim is still indefinite if a person of ordinary skill in the art cannot translate the definition into meaningfully precise claim

scope."). Although Plaintiffs have been unable to ascribe a clear meaning to "fully encapsulated," it is clear from the specification that "full" encapsulation must be something other than "partial" encapsulation. Whether or not a person of skill in the art could determine the scope of the invention with reasonable certainty is an inquiry for expert discovery and trial. Indeed, the parties ***agreed*** to defer indefiniteness arguments. D.I. 129 at 2.[36]

* * *

Therefore, based on the inventors' express definition, "fully encapsulated" should be construed as "fully, as distinct from partially, encapsulated."

3. Plaintiffs' Reply Position

Moderna has no response to the bulk of the intrinsic evidence that compels Plaintiffs' construction. Br. 67-68. The specification provides that "full" encapsulation requires the mRNA to be "within" or "in" the lipid vesicles, *i.e.*, ***contained inside*** them. *See* '651 patent, 9:36-39 (70-80% of a nucleic acid is located "***within*** the lipid vesicle"), 2:30-33 (therapeutic product, such as mRNA, is "encapsulated ***in***" the lipid vesicle). The file history supports Plaintiffs' construction as well. During prosecution, Plaintiffs repeatedly distinguished claims requiring "fully encapsulated" mRNA over prior art, in which "little, if any, of the DNA payload is encapsulated ***within*** the preformed cationic liposomes." J.A. 16 (10/22/2014 Response), 7; *see also* Br. 66-68.

The intrinsic evidence also confirms that encapsulation efficiency is used as a measure of percent fully encapsulated. The specification discloses encapsulation efficiency percentages that track the claims' "fully encapsulated" percentages. Br. 65. And during prosecution, Plaintiffs and

[36] Plaintiffs also "reserve[d]" the right to defend against indefiniteness "on the basis of waiver." D.I. 129 at 2. Plaintiffs thus both argue that Moderna's construction "manufactures" indefiniteness, while also stating Moderna would have waived any indefiniteness arguments if it did not raise it now.

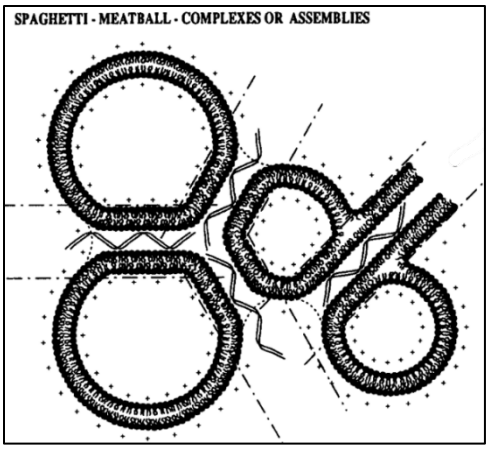
the Examiner repeatedly distinguished claims reciting percentages of "fully encapsulated" mRNA from the prior art based on the encapsulation efficiencies required. Br. 66-67. Those statements only make sense with Plaintiffs' construction of "fully encapsulated." Moderna offers no explanation for why these arguments were sufficient to overcome the Examiner's rejections if "fully encapsulated" meant "fully, as distinct from partially encapsulated," as Moderna contends.

Moderna makes four arguments in support of its construction, none of which can overcome the undisputed intrinsic record or obscure that Moderna's own proposed construction provides no clarity on what "fully encapsulated" means. Moderna's thinly veiled attempt to conjure an indefiniteness argument should thus be rejected, and Plaintiffs' construction adopted.

a. The definition of "lipid encapsulated" is irrelevant and provides no clarity on what it means for mRNA to be "fully encapsulated."

Moderna incorrectly asserts that the specification ***defines*** "fully encapsulated." Br. 70-71, 73. The only definition Moderna cites is for a different term, "lipid encapsulated," which appears nowhere in the claims. Moreover, the specification's disclosure that "lipid encapsulated" can refer to "full" or "partial" encapsulation does not define what "fully encapsulated" means, any more than a statement that "exercise" can refer to "aerobic" or "anaerobic" exercise defines "aerobic exercise." Moderna's construction improperly specifies only what "fully encapsulated" ***is not***, rather than what it ***is***. *E.g.*, *Funai Elec. Co., Ltd. v. Daewoo Elecs. Corp.*, 616 F.3d 1357, 1366 (Fed. Cir. 2010) (construction should "aid[] the court and the jury in understanding the term as it is used in the claimed invention"); *Endoheart*, 2016 WL 1270127 at *5 (rejecting construction that "confuses rather than clarifies the claim term"); *Intel Corp. v. Qualcomm Inc.*, 21 F.4th 801, 812 (Fed. Cir. 2021) (finding Board's "purely negative" construction of "hardware buffer" inadequate because it adds "uncertainty").

b. Plaintiffs' construction gives meaning to the word "fully" and is supported by the intrinsic evidence.



Moderna also is wrong that Plaintiffs read "fully" out of the claims. Br. 71-72. Plaintiffs and Moderna agree that "fully" refers not to the amount of encapsulated mRNA, but instead to its "state or location." Br. 70. "Fully" encapsulated mRNA is located inside the lipid vesicles, not outside of them. Br. 67-68. And consistent with the specification, "partially" encapsulated mRNA is outside of lipid vesicles, *e.g.*, "contained within a relatively disordered lipid mixture." '651 patent, 5:33-37. As Dr. Thompson explained, J.A. 7 (Thompson) ¶ 19; J.A. 34, 364, such a "partially encapsulated" mRNA can be visualized as shown here, with the mRNA corresponding to the individual strands (the "spaghetti") within the relatively disordered lipid mixture (the "meatballs").

Moderna irrelevantly notes that the phrase "contained inside" appears nowhere in the specification, Br. 71-72. The law does not require that claim construction language appear *ipsis verbis* in the specification. *In re Edwards*, 568 F.2d 1349, 1351-1352 (C.C.P.A. 1978). And, as discussed above, the intrinsic record refers repeatedly to "fully encapsulated" mRNA as being located "within" or "in" the lipid vesicles, which means "contained inside" in plain English.

c. The file history confirms Plaintiffs' construction.

Moderna diminishes the file history that supports Plaintiffs' construction, arguing that Plaintiffs distinguished the prior art by contrasting encapsulation generally (*i.e.*, full and partial encapsulation) with "association" (*i.e.*, no encapsulation at all). Br. 73. But Moderna's argument finds no support in the record and makes little sense, given that the pending claims recited "fully

encapsulated" percentages of mRNA, not "encapsulated mRNA" generally.

Moreover, Plaintiffs expressly distinguished the prior art based on the "fully encapsulated" claim limitation, including in both office action responses Moderna cites. J.A. 16 (10/22/2014 Response), 10 (prior art fails to teach "the particular lipid components recited in the present claims to ***fully encapsulate*** and successfully deliver mRNA"); J.A. 19 (5/12/2015 Response), 6 (prior art does not disclose "a lipid vesicle of the present invention comprising ***fully encapsulated*** mRNA"). Additionally, Plaintiffs argued that the prior art does not disclose "fully encapsulated" nucleic acid, but instead describes "complexes with DNA called lipoplexes" (J.A. 19 (5/12/2015 Response), 6), in which the nucleic acid is "contained within a relatively disordered lipid mixture," not inside lipid vesicles as full encapsulation requires. '651 patent, 5:35-37; J.A. 7 (Thompson) ¶¶ 95-99.

d. Plaintiffs' construction does not inject method limitations.

Moderna's assertion that Plaintiffs' construction injects method steps into composition claims likewise is wrong. Br. 73-74. The claim is not limited to any particular nucleic acid encapsulation process; any encapsulation process that results in the claimed % fully encapsulated can be used.[37] The percentage of "fully encapsulated" mRNA is a characteristic of the claimed "lipid vesicle formulation." That the POSA would assess this characteristic by measuring encapsulation efficiency, J.A. 7 (Thompson) ¶¶ 75, 77, 91, does not add a method step to the claims. Indeed, composition claims often recite ingredient amounts; the mere fact that the amount is measured in some way (*e.g.*, by weighing) cannot transform the claim into a process claim. *E.g.*, *3M Innovative Props. Co. v. Avery Dennison Corp.*, 350 F.3d 1365, 1371 (Fed. Cir. 2003) ("[E]ven words of limitation that can connote with equal force a structural characteristic of the product or a

[37] Moderna invites the Court to address one of its invalidity defenses in asserting, baselessly, that the claims cover formulations with "poor encapsulation efficiency (*e.g.*, 30%)" where the "free and unencapsulated nucleic acid was filtered out." Br. 74. That issue is not before the Court in the present claim construction dispute.

process of manufacture are commonly and by default interpreted in their structural sense").

Nor does Moderna's reliance on claim 5 of U.S. Patent No. 7,901,708, help its argument that "encapsulation efficiency" refers to "methods of encapsulating nucleic acids." Br. 73. In that patent, claim 1 recites a process for producing lipid vesicles encapsulating nucleic acids and dependent claim 5 (which Moderna cites) specifies that the resulting lipid vesicles exhibit certain encapsulation efficiency percentages. J.A. 53, claim 5. But dependent claim 5 does not refer to "encapsulation efficiency" as a step in the process of claim 1 at all. Rather, consistent with the intrinsic record of the '651 patent, encapsulation efficiency refers to a characteristic of the product (lipid vesicles) of claim 5 of the '708 patent, measured by techniques known in the art, ***following*** encapsulation of the nucleic acid in the vesicles. J.A. 7 (Thompson) ¶¶ 77, 91.

Plaintiffs' construction defines "fully encapsulated" with clarity and is consistent with the intrinsic and extrinsic record. Moderna's proposed construction, on the other hand, offers no clarity on what "fully encapsulated" actually means and should be rejected.

4. Moderna's Sur-reply Position

The '651 patent defines "lipid encapsulated" as "a lipid formulation which provides a compound with full encapsulation, partial encapsulation, or both." J.A. 5 at 5:38–40. This is the ***only*** use of the term "full" in the context of lipid encapsulation in the '651 patent. This cannot be "***irrelevant***" as Plaintiffs suggest. Br. at 76–77. The specification is paramount to understanding the claim. Indeed, Plaintiffs' expert relies on the same part of the specification but ignores the use of "full." J.A. 7 ¶¶ 94–95, 99 (citing 5:38–40). Plaintiffs' other cited passages do not refer to "full" or "fully" encapsulated, and one does not even refer to "encapsulation." Br. at 75 (citing 9:36-39, 2:30-33). Similarly, none of Plaintiffs' prosecution citations include ***any*** explanation of what "fully" encapsulated meant in terms of "location" or type of encapsulation, let alone use Plaintiffs' construction to distinguish the claims. Br. at 75–76 (citing J.A. 16 at 7). As Plaintiffs implicitly

concede, Arbutus at most distinguished the '651 claims from "lipoplexes." Br. at 78. "Lipoplexes" are not discussed in the '651 patent, nor did Arbutus link "lipoplexes" in the prior art to the specification. In short, Plaintiffs' construction is not supported by the intrinsic record.

Plaintiffs argue that Moderna imports a negative limitation. *Id*. at 76–77. But the ***inventors*** distinguished between "full" and "partial" encapsulation, not Moderna. *Id.* at 70–72. Indeed, Dr. Thompson agreed that "full" and "partial" encapsulation are distinct concepts (*i.e.*, fully encapsulated means ***not*** partially encapsulated). J.A. 88 at 133:3–22. Even if this were a negative limitation, the specification confirms that the inventors defined "full encapsulation" by distinguishing from "partial encapsulation." *See SkinMedica*, 2011 WL 2066619, at *6–*8 (construing term to exclude characteristics distinguished in specification), *aff'd*, 727 F.3d 1187.

Plaintiffs' cited cases only support Moderna's construction. In *Intel*, the Federal Circuit vacated a construction where the PTAB "failed to tie [it] . . . to the actual invention described in the specification." 21 F.4th at 804. Here, Moderna's construction ***is*** supported by the specification, where the inventors—not Moderna—contrasted "full" with "partial encapsulation." Similarly, *Funai* and *Endoheart* emphasize the specification's importance in construing terms. *Funai*, 616 F.3d at 1366 (upholding construction based on comparative language in specification); *Endoheart*, 2016 WL 1270127 at *5 (declining construction to include words not supported by specification).

Plaintiffs and Dr. Thompson rely heavily on a figure found only in extrinsic evidence (Br. at 77; J.A. 7 ¶¶ 19, 93–94),[38] claiming that it shows "partially encapsulated" nucleic acid ***not*** "fully encapsulated." Br. at 77; J.A. 7 ¶ 94; J.A. 88 at 132:14–133:22, 134:17–135:10. But Plaintiffs' proposed construction has a glaring deficiency—that a nucleic acid could be partially ***or*** fully

[38] Plaintiffs have retreated from suggesting that Claim 1 recites ***methods*** that achieve certain encapsulation efficiencies. Br. at 64–65; Br. at 78–79; J.A. 88 at 114:3–24.

"contained inside" a lipid vesicle.[39] Thus, their "fully encapsulated" construction reads onto "partially encapsulated" nucleic acids, despite the clear distinction between the two in the specification. Plaintiffs' proposed construction does not give meaning to "fully" or provide clarity to the claims. Reading out the word "fully" is disfavored. Br. at 72–73; *see also Intel*, 21 F.4th at 810. Therefore, the Court should adopt Moderna's proposed construction.

[39] In his deposition, Dr. Thompson acknowledged a phenomenon where a nucleic acid protrudes through the lipid shell, resulting in the nucleic acid having a part outside, or "exposed," and another part entrapped inside the lipid vesicle. J.A. 88 at 138:10–139:11.

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CERTIFICATION REGARDING PAGE LIMITS

We, undersigned counsel for the parties, hereby certify that the parties' briefs served pursuant to Paragraph 12 of the Scheduling Order (D.I. 72), as amended, complied with the page limits set forth therein, and that the foregoing Joint Claim Construction Brief exceeds eighty (80) pages due to the presence of figures and extra page breaks due to formatting issues.

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